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THE RELATION BETWEEN CLINICAL AND LABORATORY DATA IN TUBERCULOSIS.*

By Alfred H. Caulfeild, M. B.

(Department of Medical Research, University of Toronto.)

Unforeseen interruptions in our work must be my apology for the incompleteness of this paper. Since August, 1914, we have been able to undertake very few new cases, and have made very few further observations on our old cases, so that at present I have only a few data to present in addition to those which we published in July in the Transactions of the tenth annual meeting of the National Association for the Study and Prevention of Tuberculosis. During that month we had started a card index of the cases in which the laboratory results had aided us in forming a more definite opinion than might have been possible by clinical methods alone. This was done merely that we might be more certain of keeping in closer touch with the subsequent history of these patients, as they seem to drift about and easily get out of reach. Unfortunately it has been impossible to keep this up to date and the partial report which one of the visiting nurses was able to get in December leaves out a great deal that was essential. Under these circumstances I thought a very fair method of checking the value of the work would be to give the subsequent history of those cases published as typical examples in July.

We have sought to show a correlation between certain laboratory results and the clinical course of tuberculosis by performing these reactions in a more or less routine fashion upon the patients presenting themselves at the Tuberculosis Clinic of the Toronto General Hospital, and also upon certain patients sent us for this particular purpose. All told, very nearly 500 cases have been investigated in this fashion, although, as the work has now been twice interrupted, the number which has been followed consistently is greatly under this figure. I should add, perhaps, that in tuberculosis cases showing changes will be found only by following a large number of patients for a comparatively long period of time. It is of

*Read before the Laennec Society, Johns Hopkins Hospital, January 25, 1915.

course this necessity of following a large number of cases in order to demonstrate a few instances of marked correlation between the laboratory results and the comparatively sudden change in the clinical course that makes the work long and tedious.

The two means of obtaining data to which I will refer as laboratory methods to-night have been:

(1) Estimation of tuberculin sensitiveness (or hypersensitiveness).

(2) Test-tube reactions with the patient's serum—an alcohol-ether extract of *B. tuberculosis*, as antigen, and an ordinary hæmolytic system, such as is used for complement fixation, being employed.

These test-tube results divide themselves into three end-reactions as follows:

(a) Inhibitive reaction.

(b) Fixation reaction.

(c) Indifferent reaction (negative).

This is a sort of modification and enlargement of the Bordet-Gengou complement-fixation phenomenon and I might explain the nomenclature by quoting from previous papers on this method:

The technique adopted to demonstrate the different end-results, which in the case of the inhibition reaction is a phenomenon the reverse of true complement fixation, is based upon the fact that all antigens are capable of non-specifically absorbing complement in various degrees. Now, if to an appropriate series of antigen dilutions, whose complement-absorbing capacities are quantitatively shown, sera are added, it will be found that the serum may show any of the following results:

(1) True complement fixation (the demonstration of this taking place in antigen dilutions which absorb only minimal parts of a unit of complement).

(2) Indifferent result (the addition of serum does not affect the quantity of complement absorbable by the same amount of antigen by itself).

(3) Inhibitive reaction (this serum so reacts with antigen that, in contrast to the same amount of antigen by itself, it absorbs less complement. Naturally then the different end-results are quantitative and must be so read).

The estimation of tuberculin sensitiveness has been made by using a definite quantity of tuberculin cutaneously and latterly intra-cutaneously (the von Pirquet and Mantoux methods), and recording the degree by measuring the result. These data showing that the tuberculin sensitiveness varies very markedly during the course of the disease is also supplemented by similar results in clinically non-tuberculous persons. So far as I have noticed, ours is the only report showing such a curve for the latter, although many others have also shown this in the tuberculous, a recent paper being one by James B. Holmes. In a previous report we have shown curves of the tuberculin sensitiveness in both the tuberculous and non-tuberculous that represent a duration of four to five years. One great difference in the curves that we have thus obtained and those published by others lies in the fact that our estimations have been made at such long intervals that it was impossible for the previous use of the tuberculin to affect the subsequent result, which might have been a theoretical contention.

Generally speaking, patients whose sera give an inhibitive reaction are doing well at the time. This seems more marked when their tuberculin sensitiveness (hypersensitiveness) is either very marked or very slight. Not all patients whose sera give the indifferent (negative) result are retrogressing, but they usually are, or are remaining *in statu quo*. Again, all patients whose sera maintain the complement-fixation result seem to go rapidly backwards. I should add that of the 14 persons in whose sera this latter reaction has been found only one, so far as we know, has continuously maintained it. Apart from this general correlation the most noticeable fact is that when a marked change in the test-tube result with a patient's serum is demonstrated, this is nearly always followed by a change in the clinical course. I say nearly always, because it is not always possible to be quite certain of this clinically, while again a subsequent test of the serum may give the original reaction. These test-tube results vary quantitatively, and one may be in doubt if the change is a marked one.

Having briefly outlined the type of the laboratory and clinical correlation, I shall now proceed to deal with these subsequent histories, and then attempt to outline the further researches which I now hope we shall be able to finish.

Results Obtained on Clinical Normals.

Work with this material was being continued because we believe tuberculin sensitiveness and the test-tube serum reactions result from tuberculous infection. Normals must every now and then fail to become clinically tuberculous, because they successfully resist implantations or reactivation, and not because these events do not happen. We had hoped that, if a sufficient number were followed in this way, variations would be found and possibly a correlation obtained. In the list of 18 cases so observed four gave variations. The variations obtained in one of these cases (No. 4) led to a gradual suspicion of tuberculosis which was confirmed clinically and bacteriologically. This patient, without entirely stopping his work, has remained free from any marked clinical evidence of the disease, and, although now lost to observation, is known to be well and working; indeed, he has never ceased work. Case 2 showed the most marked variations during 1910 and 1911, when clinical tuberculosis was suspected, but not confirmed. Since then the variations have ceased, and at present there have been no symptoms suggesting tuberculosis. Of the two remaining cases one (No. 12) complained at the time of the variations of definite discomfort in his knee. This has since disappeared. No further observations have been made, so that any discussion could be only theoretical, and would bring up the possibility of the tubercle bacillus as a possible cause of rheumatic-like complaints.

Results Obtained in Cases of Definite Exposure.

Our purpose with this sort of material was to demonstrate the results which would be obtained in persons who had definitely been exposed, and in whom the exposure was followed

by no apparent clinical manifestations. If our theory were correct all, or nearly all, of these cases should show, as well as tuberculin sensitiveness, an inhibitive serum reaction.

Of the seven cases published all gave an inhibitive reaction, although in two it was not marked. One case cannot be traced; of the remaining six, none shows any evidence of tuberculosis. The tuberculin sensitiveness varied a good deal, as did also the probable duration of the exposure. In one case, where the exposure was intimate and of short duration, a rise in the tuberculin sensitiveness was shown following the exposure.

Subsequent Histories of Cases Giving Doubtful Evidence of Pulmonary Tuberculosis.

The examples published were from a list of patients in whom a diagnosis of tuberculosis could neither be excluded nor confirmed with certainty by clinical methods. The logic of the laboratory results helping in a diagnosis lies in the value of marked changes being found in the reactions in repeated tests, especially if these correspond to changes in the clinical welfare, as we find they do, in the definitely tuberculous.

Five cases have been cited above as examples. In cases 1 and 2 tuberculosis was excluded by means of the laboratory results; both patients at present are alive and well and are working or are capable of doing so.

In Cases 3, 4 and 5 tuberculosis was diagnosed as being a cause of the clinical picture. Case 3 got worse and returned to Russia. Case 4 is now in the hospital and tuberculosis is only slightly more evident on physical examination than formerly, but no other diagnosis has been arrived at, nor have any further tests been made. In Case 5 we were searching for a differential diagnosis for masses which could be palpated in the abdomen. Tuberculosis was diagnosed and new growths were excluded. The enlargements are about the same and the patient is going to school at the present time.

At the time these five cases were selected as examples we had drawn up a much longer list, but thought five would be sufficient. One of those that would have served equally well as an illustration has shown such a marked change subsequently that I will now add this history (No. 2822) as a further illustration. On April 24, 1914, the diagnosis of tuberculosis was aided by the laboratory results and a further note of "apparent recovery" was added to the history. This patient, although told to report monthly or at any time he did not feel well, did not come to the clinic until November. He then gave a history of having felt sick for some time and his condition was found to have advanced to such an extent that an artificial pneumothorax was considered.

In this class of material I feel that the value of the methods is to be judged in two ways: (1) Of those cases in which we have excluded tuberculosis, after six months or more, a high percentage should still be clinically free. It is of course possible that subsequently a few may contract tuberculosis. (2) Of those patients in whom biologically active tuberculosis was diagnosed, a very high percentage should subsequently show definite tuberculosis.

Subsequent Histories of the Definitely Tuberculous

To these cases which have been published there can, of course, be very little added. Some of the patients have remained *in statu quo*, others have shown progress or retrogression, but not many more observations have been made on these particular cases. Here again I do feel it essential that not only should there be examples in which the correlation is excellent, but that there should also be practically no instances in which the laboratory results, when taken with the apparent clinical findings, would have been misleading. In a few cases, in which the clinical course has not seemed to correspond as closely as could be desired with the indications given by the laboratory results, it has been difficult to decide whether the laboratory results were really to blame. Sometimes other complications have obscured judgment and sometimes the laboratory results, as shown by repetition, have altered. I can only state that, as far as we have been able to interpret the results, we have not been misled to any important degree. This work has included a great number of severe tests, as, for instance, the differential diagnosis in cases of suspected miliary tuberculosis. In this sort of material so far all our results have been confirmed by the post-mortem diagnosis.

From continued observation, utilizing both the two laboratory and the clinical findings, we have come to regard a marked inhibitive serum reaction as significant of high resistance to the tubercle bacillus, and particularly so if the tuberculin sensitiveness is either marked or minimal. Whether a marked inhibitive serum reaction can be found with a non-active tuberculosis cannot possibly be satisfactorily determined by observations on human beings. In fact the actual proof of the relation of tuberculin sensitiveness and the serum reaction to the clinical progress can only be proved by experimental work with animals, and it is the attempt that we are making in this direction that I will now try to outline.

Previous work with the small laboratory animals had failed to show any method of inoculation whereby the inhibitive reaction of the serum could be produced. When we were forced to give up the convenient guinea-pig and rabbit, cattle naturally suggested themselves, and in November, 1912, we collected samples of blood from different cattle, and at the same time made an intracutaneous or subcutaneous tuberculin test, or both. Thirty-two animals have been so examined and certain of these repeatedly tested. The results showed correlated data very comparable to those obtained with human beings. In only one instance did we obtain an indifferent reaction with an absolutely tuberculin-negative reaction. As the animal was an expensive thoroughbred at the Guelph Experimental Farm it was not autopsied. One animal, a Jersey cow, showed marked complement fixation on four different occasions between July and November, 1914. This cow retrogressed so rapidly from July that she had to be killed in November, and the autopsy showed very extensive tuberculosis. The tuberculin reactions had always been very marked. Moreover, this was the only animal that gave complement fixation, all the others showing

either the indifferent or various degrees of the inhibitive serum reaction. We have experimentally inoculated with living tubercle bacilli three healthy looking animals, each having shown a different set of laboratory results, and, to judge by the results after the use of the intracutaneous tuberculin test and the test-tube serum reactions, it is evident that following the inoculation different animals respond differently.

Encouraged by this we have produced also pleural exudates in certain of the inoculated animals and are attempting to determine whether it is possible that any immune substance may be present in either the blood serum or the pleural exudates of any of these animals, which under a similar inoculation have responded in an apparently different way biologically.

In closing I should like to refer to certain publications by Calmette,[1] in which he describes a reaction which he calls *inhibiteur*. Although there are differences in the technique and antigens, many of the conditions in which Calmette finds his inhibitive reaction are those in which, I believe, the reaction I have called "inhibitive" might also be found. This is particularly noticeable to me in one of his fuller communications.

DISCUSSION.

DR. HAMMAN: There are a number of interesting aspects from which Dr. Caulfeild's paper might be viewed. As regards the specificity of his test and its relation biologically to complement absorption and other serum reactions, only one actively engaged in studying these questions would be qualified to speak. Dr. Caulfeild has said that he is convinced from his results of the absolute specificity of the reaction and from the clinical standpoint the results of his work are of great interest. For many years we have looked to biological tests to help us in the diagnosis of tuberculosis and in its treatment. The many biological tests that have been tried have so far been of little clinical value. Precipitin reactions, agglutination reactions, opsonin reactions and complement fixation have all been tried on a large scale and though biologically their specificity may be certain, still clinically they have been of little value in the study of tuberculous disease. This is no doubt due to the complex nature of tuberculosis from the clinical standpoint, the complexity, I take it, consisting merely in this fact, that infection and disease in tuberculosis are not synonymous terms as they are in practically all other infections. It must be remembered that the tuberculin reaction is just as delicate and just as specific as the Wassermann reaction and the reason it has less clinical value is because in the clinic we must separate tuberculous infection from tuberculous disease, whereas no such distinction is necessary in syphilis.

As regards complement fixation, I admit that I am particularly influenced by the work of Roemer when I say that it has been of as little value in the study of tuberculosis experimentally as it has in clinical studies. Roemer has tried out the test very thoroughly in animals and has found that there is no relation between the presence or absence or the degree of complement fixation and the severity and extent of the disease in animals, or of resistance to superinfection. I have myself come gradually to feel that immunity in tuberculosis is more closely bound up with hypersensitiveness than with any protective body or bodies in the serum. I realize that at present there is in some quarters a tendency to lay more emphasis than has recently been done upon the humoral aspects of immunity in tuberculosis.

I am particularly interested in what Dr. Caulfeild has said about the relation of his test to the tuberculin test. I understood him to say that in patients showing a well-marked reverse reaction the outlook was favorable, whether they reacted severely or mildly to tuberculin. We have been very much interested in the relation of tuberculin hypersensitiveness to prognosis in tuberculosis and we have opposed the attitude that is commonly accepted, namely, that the higher the degree of hypersensitiveness the more resistant the patients and the more likely they are to improve. Our work has convinced us that, other things being equal, those who have a low tuberculin hypersensitiveness are in a better way to recover than those in whom the hypersensitiveness is very high. This conclusion, however, is only relative, for at certain periods of the disease a high tuberculin sensitiveness may be associated with a very good prognosis. The question is complicated and I cannot go into it in detail. I wish merely to say that if Dr. Caulfeild's reaction will tell us which patients are likely to do well, whether they have a high or a low tuberculin hypersensitiveness, it will prove to be a very valuable clinical aid in our study of the disease.

DR. CAULFEILD: Dr. Hamman has touched on two very important features. I feel very strongly myself that we shall not get any one serological reaction which is going to be pathognomonic of the disease. Therefore, one must get a combination of serological or biological results which will outline the patient's resistance. That is what I have been more or less hoping.

Dr. Hamman speaks about tuberculin hypersensitiveness and lack of hypersensitiveness. I always have felt that, because of the correlation between the two groups, one very often gets in an absolutely clinical normal a very high degree of tuberculin sensitiveness, which must indicate that that patient has successfully resisted tuberculosis.

[1] Calmette et Massol: Ann. Instit. Pasteur, 1914, XXVIII, 338.

SOME CULTURAL STUDIES ON THE TUBERCLE BACILLUS.*

By S. A. PETROFF,

Adirondack Cottage Sanitarium.

More than thirty years have passed since Koch discovered the tubercle bacillus. By infecting guinea-pigs with tuberculous material he was enabled to cultivate from the spleen the organism in serum media. It took eight weeks, however, for the growth to appear. At that time the tubercle bacillus could be isolated in only one way—through infected tissues. In 1909 Uhlenhuth and Kersten, in a report on the bactericidal action exerted by antiformin on many organisms, called particular attention to the fact that it had little or no effect on the tubercle bacillus. The same authors were the first to isolate and cultivate the organism by the aid of this compound. Dr. Lawrason Brown, at the Adirondack Cottage Sanitarium, modified somewhat their method and, with Smith, reported the successful isolation and cultivation of tubercle bacilli from forty-five sputa. Some later workers, following their method, failed to cultivate *B. tuberculosis*, but the failure was due not to the

* This investigation was made possible by the Harriman-Sage Fund. Paper read before the Laennec Society, January 25, 1915.

method, but to faulty technique. A 30 per cent antiformin was used, a solution of fairly high specific gravity. Equal parts of 30 per cent antiformin and sputum were shaken well and incubated. The sediment was then washed with sterile water and again centrifugalized. This procedure was repeated. At times the method was very effective, but did not prove of great practical value on account of the elaborate technique involved. In repeated washings, many of the organisms were not thrown down; in many instances we have found tubercle bacilli on the surface, some in the fluid and some in the sediment; moreover, the possibility of contamination was great. Repeated trials to apply this method to cultivating the tubercle bacilli from the feces failed to give a positive growth free from contaminating organisms. In the spring of 1914, at the suggestion of Dr. Lawrason Brown, we started this investigation from the point where he had left off, and without his hearty co-operation this work could not have been so successfully accomplished.

The effect of certain aniline dyes on the development of the bacterial cell was known even in 1886, when the botanist Pfeiffer demonstrated the harmful effect of these dyes upon higher plants. Rozsahegyi pointed out their effects upon different bacteria, and these pioneers were followed by Cornil, Babès, Penzoldt, Stilling and many others, who published very interesting results of investigations, although none of them appreciated the connection between these properties of the dyes and their practical application in bacteriology. Churchman was the first, to my knowledge, to study this subject systematically and in the course of his work made a very practical discovery. It was the work of Churchman, followed by that of Simons and other investigators, which suggested the use of aniline dyes in the isolation of the tubercle bacillus.

After it had been demonstrated that tubercle bacilli would grow in a medium containing gentian violet 1 to 50,000, an attempt was made to cultivate them directly from the sputum. Only a few Gram-positive organisms appeared in the tubes. Of these organisms some were staphylococci and others streptococci. They were carefully studied. Gentian violet does not possess properties inhibitory to these organisms even in a dilution of 1 to 1000. For the elimination of them several alkalies with bactericidal properties were studied. In selecting the alkali we tried to find one that could be easily neutralized, bearing in mind that the resulting salt must not affect the tubercle bacilli. Sodium hydroxide proved of value. But before proceeding we carried out a small experiment on the bactericidal action on tubercle bacilli exerted by this alkali. A 4 per cent solution of sodium hydroxide will not destroy the tubercle bacillus when incubated at body temperature for 24 hours, and, as this alkali possesses a high bactericidal property against all streptococci and staphylococci, it was selected.

The next step was to determine what dilution of gentian violet was most favorable for the development of the tubercle bacillus. A series of media containing different dilutions of gentian violet, varying from 1 to 1000 to 1 to 100,000, was used. A dilution of 1 to 10,000 gave the best results.

In my last communication, in the Journal of Experimental Medicine for January, 1915, may be found the details of all this work. Here I shall give very briefly the preparation of the medium and also the method of isolating and cultivating the organisms from the sputum and the feces.

After many trials it was found that a medium containing whole egg, beef or preferably veal juice and gentian violet gives uniformly positive results. This medium contains: One part of meat juice, two parts of the egg (white and yolk), gentian violet sufficient to make a solution of 1 to 10,000.

I. *Meat Juice.*—Five hundred grams of beef or veal are infused in 500 cc. of a 15 per cent solution of glycerine in water. Twenty-four hours later the meat is squeezed in a sterile press and the infusion collected in a sterile beaker.

II. *Eggs.*—Sterilize the shells of the eggs by immersion for ten minutes in 70 per cent alcohol or by pouring hot water upon them. Break the eggs into a sterile beaker and after mixing well, filter through sterile gauze. Add one part by volume of meat juice to two parts of egg.

III. *Gentian Violet.*—Add sufficient 1 per cent alcoholic solution of gentian violet to make a proportion of 1 to 10,000.

After mixing well for a few minutes the medium is tubed as usual and inspissated for three successive days, first at 85° C., until all the medium is solidified, and on the second and third days for one hour at 75° C. Lately we have found that even a temperature of 100° C. will not decrease the nutritive properties of the medium.

We have noticed a great variation in the gentian violet, that is, some samples gave a deeper color to the medium than others. This variation we cannot at this time explain.

Method of Isolating Tubercle Bacilli from the Sputum.

To obtain rapid and uniform results, fresh sputum must be used. Equal parts of sputum and 3 per cent sodium hydroxide are shaken well and incubated at 38° C. for from 15 to 30 minutes, the time for incubation depending on the consistency of the sputum. This mixture is then neutralized to litmus paper with hydrochloric acid and centrifugalized at high speed for 10 minutes, the supernatant fluid is decanted and the sediment inoculated into the medium described above.

We have controlled the gentian violet medium with one made of an egg and meat juice only. Many of the tubes containing the plain medium were contaminated, and the contaminating organism was mostly *B. subtilis*. On the other hand, the gentian violet medium was free from these contaminating organisms. Occasionally we have met with some molds which are not inhibited by the gentian violet.

Method of Isolating Tubercle Bacilli from the Feces.

It is an entirely different problem to isolate and cultivate tubercle bacilli from the feces. Here we have many spore-forming organisms which resist the action of sodium hydroxide. Here the time of incubation plays a more important part than the concentration of sodium hydroxide. Feces are collected in wide-mouthed jars, a fresh morning specimen giving the best results. The feces are diluted with three volumes of water, mixed well and then filtered through several thicknesses of

gauze to remove solid food particles. The filtrate is saturated with sodium chloride and left undisturbed for a half hour. At the end of that time all bacteria will be found floating. This floating film is collected with a deflagration spoon in a wide-mouthed bottle, and an equal volume of normal sodium hydroxide is added. This is shaken well and left in the incubator, at 38° C., for three hours. It should be shaken every half hour, neutralized to sterile litmus paper with normal hydrochloric acid, centrifugalized, and the sediment inoculated into the several tubes containing the medium.

The appearance of the growths was not uniform. In the case of the sputum, in one instance we obtained a visible growth on the fifth day, but in others the growth was not seen until the 14th or 15th day. The average time for the appearance of a visible growth was nine or ten days. By close observation, we noticed that the moisture of the medium influenced to some extent the development of the organism. At the present time, it is our routine, after inoculation, to leave the tubes in the incubator for a few days, until the moisture carried from the centrifuge tubes is completely absorbed by the medium, or evaporated. Then the tubes are paraffined to prevent the further drying of the medium.

The temperature of the thermostat is of considerable importance. A constant temperature of 38.5° C., is most suitable for the rapid growth of the tubercle bacillus.

The growth from the feces appeared much more slowly than that from the sputum. On an average from two to three weeks elapsed before the growth was perceptible. In all probability many of the tubercle bacilli are dead or weakened when passed with the feces.

A study was carried out with glycerine-agar and egg-meat-juice media, for the purpose of observing the differences in cultural characteristics on the two media. A series of tubes of these two media, containing gentian violet in the proportion of 1 to 10,000 to 1 to 100,000, was used. Several distinct types were inoculated in the usual way and incubated. The growth in the egg medium was abundant at the end of the fifth day, whereas the agar cultures gave a scant growth. Some of the strains decolorized the agar as well as the egg medium, while in others, which did not develop so rapidly, the growth appeared in the tubes to be stained violet. Upon microscopical examination of the latter strains, however, only a few of the organisms were found to have absorbed the stain. Most of the dye appeared to be adherent to the bacterial cell and subcultures gave no positive growth. Churchman, in studying *B. typhosus* on gentian violet media, observed the same phenomenon, but on subculturing he obtained an abundant growth. *B. tuberculosis* will not continue to grow on gentian violet media and all subcultures after isolation must be carried on in a dye-free medium. Only a few types of tubercle bacilli will grow in glycerine-agar-gentian-violet media. When grown upon media containing the dye, a type that decolorizes the media is of longer life than one which has selective properties for the dye. What the factors are which bring about the decolorization of the media we are not at present able to state.

A comparative study was also carried out with methylene blue. The dye has no influence upon the growth of the tubercle bacillus in a dilution of 1 to 100,000. The growth appears the same as on a dye-free medium. Upon microscopic examination we find that the dye adheres to only a few bacterial cells. When we use this dye in the proportion of 1 to 50,000 the growth seems to be retarded for several days. The whole mass used for inoculation appears to be blue. Upon microscopic examination we find that a good many of the organisms have absorbed the dye. If we examine the tube a week later we find that the primary inoculation is still blue, while the medium surrounding and below this area is considerably decolorized and there is marked evidence of a new growth. This new growth does not appear to be blue, but upon microscopical examination we find many of the individual organisms stained in different shades of blue, some darker than others. Is it possible that, when the bacterial cell absorbs the stain, it is not killed, but simply that the process of reproduction is retarded for a while and then, when it divides into twos or threes, on account of the division, the staining is much lighter? Possibly other explanations may be offered; that the dead organisms are stained dark blue; that the light ones are not dead, and that after absorbing more dye they are killed. This phenomenon is under consideration and further investigation may throw some more definite light on the problem. The growth is completely inhibited if the medium contains the dye in the proportion of 1 to 25,000. The bacterial cells are uniformly stained very dark blue.

It is probable that there is more than one type of human tubercle bacilli. Out of 129 strains thus far isolated, we have noticed the occurrence of several apparently distinct types of organism, which may possibly be differentiated by their cultural characteristics. In some we have small pin-point colonies, which always give a scant growth on sub-culturing (this particular strain is one which has selective properties for the dyes), while others which decolorize the media produce long, spreading, veil-like, slightly raised colonies. The former type is slightly moist; the latter is dry.

Upon microscopical examination we find more striking differences. An organism that gives a very scant growth when stained by the Ziehl-Neilson method appears in minute rods, strongly resisting acid-alcohol decolorization. Granules could not be demonstrated. If we examine this type by the Gram method we find all to be in rod form.

On the other hand, if we examine a strain that gives a rapid growth we find a different picture. Stained by the Ziehl-Neilson method, only a few solid, slender, long granular rods are seen. The granules may be seen lying in the rods, sometimes close together like a string of beads, but most often separated by regular intervals. No isolated granules could be seen. The granules are only weakly stained and vary in size. By the Gram stain the preparation shows almost all the organisms in the form of granules; only an occasional solid rod. Numerous rows of granules are imbedded in a Gram-stained shadowy substance. Many single isolated granules of various sizes lie in orientation form. However, there are more than two strains, as I have already stated above.

Up to the present time we have been able to isolate and cultivate the tubercle bacillus from 129 sputa out of 135 specimens.

The method of isolation and cultivation has proved of some value in feces, as we can obtain a positive growth long before the infection is manifested in guinea-pigs. We hope to be able to use this method for isolating the tubercle bacillus from the urine.

The content of fatty acids present in tubercle bacilli, which varies greatly in different types, must, I believe, have some influence upon the virulence of the organism. At present, work is in progress upon the fatty acid content of different types, their cultural characteristics, tinctorial reactions and virulence to guinea-pigs, with the hope that it may lead to a classification of human tubercle bacilli.

In May, 1913, I reported before the National Association for the Study and Prevention of Tuberculosis a new fluid medium for the cultivation of tubercle bacilli.

Last summer I modified the medium to some extent, which made it give even better results. Briefly, I will describe the preparation of this new medium:

Five hundred grams of grated potatoes are infused in 1000 cc. of distilled water for 24 hours in the ice-chest. At the end of that time the infusion is filtered from the pulp through gauze, titrated and the reaction adjusted to 1 per cent acid. The filtrate is then heated in an Arnold sterilizer for one-half hour, until all the starch is coagulated, and then filtered through cotton. The pulp is then washed in a gauze bag under running water until free of starch (iodin test) and added to the filtrate separated from the coagulated starch, mixed well and put in the autoclave under 15 pounds pressure, filtered through filter-paper and titrated again. The final acidity must be between 0.5 and 1 per cent to phenolphthalein. Put 50 cc. in flat bottles holding 250 cc. and sterilize in the autoclave at 15 pounds pressure for half an hour. When glycerine is used in the medium, it must be sterilized in an Arnold sterilizer on three successive days. In this medium the tubercle bacilli will grow well, not only on the surface, but also in the depths of the medium.

When tubercle bacilli are grown on this medium they show marked variations; some grow in a veil form, while others will be found, as it were, piled one on top of the other. With some types many acid-fast properties are lost and after a while they will not continue to grow upon sub-culturing. It is possible that potato broth prevents to some extent the synthesis of fat present in the tubercle bacillus and that the protein is not affected.

Last summer at the suggestion of Prof. Zinsser, of New York City, a study of the antigenic properties of the growths of tubercle bacilli in this medium was undertaken and there is an indication that this line of study may be of some value in relation to complement fixation in tuberculosis. However, the work, though promising, has not as yet progressed far enough to warrant a definite conclusion.

DISCUSSION.

Dr. Barker: I think we too often harbor the idea that the technique of bacteriology is a finished subject; that there is very little to add to it. But an instance such as this described by Mr. Petroff to-night actually represents an important step forward in technique. Koch's method of isolation by plating was a fundamental contribution to the science of bacteriology, but this method of obtaining a pure culture may be an onerous business in the case of certain bacterial mixtures, and it is no wonder that bacteriologists soon tried to find shorter cuts to pure cultures. One example of a "short cut" was the "method of enrichment" devised by Schottmüller for isolating the cholera bacillus. Later examples grew out of attempts to isolate the typhoid bacillus. We all know how hard it was formerly to get pure cultures of typhoid bacilli from the feces. As bacteriological technique gradually evolved, however, it was discovered that to our media could be added certain things which would favor the growth of the typhoid bacilli or which would inhibit the growth of other bacteria in the feces.

As regards pure cultures of B. tuberculosis, we were helped first by isolation through animal inoculation, and later, still further by the antiformin treatment of suspected material. Now Mr. Petroff has given us a method, somewhat complex as described, but quite practical, I imagine, on application. The previous evolution of cultural technique was largely along one line, the effort being made to kill all organisms except the one to be isolated. Formerly it took from three to four weeks to obtain a culture of the tubercle bacillus. By this method of Mr. Petroff's we learn that they may sometimes be grown in as short a period as five days. The method would seem to be valuable for diagnostic purposes and we expect to apply it here in special cases.

Another thing that interested me in Dr. Petroff's paper was the fact that we now have the means of obtaining quickly a large number of pure cultures of B. tuberculosis from different cases, and may therefore enter upon the task of differentiating different strains. It may be that the human type of B. tuberculosis is no unity. When we think of what happened in the study of the streptococci, for example, it would not surprise us to find several different strains of human tubercle bacilli. You remember that it was believed at first that there was only one typhoid fever and that it was due to the typhoid bacillus; now we know that there are several typhoid fevers, at least four, those due respectively to B. typhosus, B. paratyphosus alpha and beta, and B. mandschuricus. It is probable, too, that several different strains of the diphtheria bacillus exist. That such special differentiations of strains of a bacterial species may not be unimportant for diagnosis and even for prognosis and therapy seems to be demonstrated by the interesting studies of Neufeld, and of Cole and Dochez, on the pneumococci of lobar pneumonia.

DIETL'S APHORISMS ON PHLEBOTOMY.*

By Norman B. Gwyn, M. D., Philadelphia.

While searching for some references upon "bleeding in pneumonia" I was confronted with the familiar name of Dietl—Joseph Dietl, of Vienna and Cracow—and found under it a long monograph, "Der Aderlass in Lungenentzündung." The 102 clinical aphorisms with which this monograph terminates form the subject matter of my paper.

"Der Aderlass" seemed to have helped to make Dietl's reputation long before his accurate description of floating kid-

* Read before the Book and Journal Club of the Medico-Chirurgical Faculty of Maryland, November 17, 1914.

ney's and the crises which bear his name. It is generally referred to as one of his chief contributions to the medical sciences and one naturally wondered, after glancing at his tables of 380 cases, if there might not be in 102 conclusions much that, at least, was interesting.

And interesting, indeed, I found them. Hippocratic at times in their truth and brevity, "Schlecht ist es wenn der Puls schon nach der ersten Venesection frei wird," might well have come from the great collection of aphorisms; while "Es gibt Pneumonien ohne Husten," "Es gibt keine chronische Pneumonien," "Die besten Pneumonien sind die bei denen nur wenig expectorirt wird," must satisfy the most vacillating student.

My interest waned somewhat on observing the date, 1848, twenty years after Louis; but the Cracow societies were still debating the "bleeding in pneumonia." Louis was still showing an affection for early bleeding and tartar emetic, and I felt, moreover, that the observations of one who at that early date could have the courage to carry through 189 cases of pneumonia, on dietetic measures alone, must not only be of interest, but of real value.

As far as one can judge, Dietl advances his arguments against blood-letting quite as if Louis' great protest had never been made. Dietl's methods are nevertheless Louis' methods—careful clinical observations ending in accurate statistical details. One senses an imitation, but hopes that the omission of any reference to Louis' work is accidental. Andral receives recognition in a reproof for his bloodiness; Laennec is completely ignored.

Dietl, as he says in his preface, had belonged to those "Strenge Antiphlogistiker" who still saw in the then bloody treatment of pneumonia their greatest triumph. Seventeen years previously, however, some taint of heresy had crept into his mind, for in 1831-3 he had tried treating severe cases of pneumonia homeopathically—"Aber es fehlte mir jedoch der Muth den naturlichen Verlauf der Krankheit ruhig abzuwarten: Mit der Zunehmenden Athemlosigkeit und Angst des Kranken stieg auch die Meinige so hoch, dass ich in mitten der präzumptiven Arzneiwirkung reuig nach der Lanzette griff, und, da diese in den meisten Fällen Erleichterung brachte, wieder zur alten Fahne schwur, der ich nun fester anhing als je."

Clinging more firmly than ever he must have remained for nearly ten years, for his *Bezirks-Krankenhaus* appointment in 1841 found him "bleeding industriously."

Bleeding, however, had a rival. For many years Tartarus stibiatus had "proved itself" with the profession, and it was being found that in some cases one did not need to bleed if large doses of tartar emetic were given. The majority of teachers, even Louis, simply went from bleeding to antimony in 20 years. Dietl stepped from bleeding to large doses of tartar emetic with vomiting, from large doses with vomiting to small doses without vomiting, from small doses to no doses (an expectant treatment of pneumonia) at a revolutionary rate. Then followed three years' observation of pneumonia treated without bleeding, and, at the end of this period, was put forth the "Aderlassung in Pneumonie," a protest larger at least and more elaborate than the great protest of Louis.

It is not my intention to review critically Dietl's monograph. It might be entertaining, for the indications of his later therapeutic nihilism are already apparent, but to most of us prolixity and a dogmatic positiveness would seem its chief characteristics; the carping reference to Andral is the only mention of any of the great teachers who had gone before him.

Almost every phase of pneumonia and the influence of bleeding upon it is taken up in the monograph; the aphorisms, of course, merely represent the crystallized result. Many have the stamp of originality, and their brevity and conciseness are attractive to a degree. They can possibly be presented more briefly and agreeably by using some reconstruction: Dietl's scheme in general can be easily followed; certain conditions of pneumonia are taken up, the application of bleeding considered, the probable or actual results detailed, and the dire effects of bleeding stated.

Not every aphorism pleases. I will try to put before you the more interesting and the most original:

ON THE PRODROMES.

The prodromes of pneumonia last longer in the young and strong, and those affected for the first time; they are shorter in the aged, weak, and those undergoing recurring attacks.

2. Venesection has the power to shorten the prodromal stages.

Dietl at no time denies that bleeding gives temporary relief.

ON THE DYSPNŒA SEEN IN THE EARLY STAGES OF PNEUMONIA.

The pneumonia patient breathes easier after completed hepatization than before.

The dyspnœa is not due to the filling of the lung cells with the plastic exudate.

Complete hepatization may limit the respiratory movements without bringing about respiratory distress.

The gaseous interchange in the lung cells is the ultimate inciter of the regulated activity of the nerve centers and the respiratory movements dependent thereupon.

On account of the enormous accumulation of fibrin as a protein-oxide a large amount of oxygen is withdrawn from the blood, and since there is reduction of the blood cells (the oxygen carriers) this, the oxygen, is never replaced in the same proportion.

12. In pneumonia less acid is taken out of the atmospheric air than is necessary for the oxidation of the venous blood and the vitalizing of the nerve centers.

13. The dyspnœa, then, must clearly be greatest during the period of the pouring out of the fibrin into the lung cells, since then the greatest call for, and the greatest deficiency of, oxygen is taking place.

15. The pneumonic's dyspnœa is preferably induced by altered chemical proportions of the blood.

17-18. Venesection should relieve dyspnœa by helping onward a continuous blood stream, more blood being driven through the capillaries in a given time, and (18) no other means of treatment suffices so to relieve dyspnœa, but (16) venesection brings about in the blood the same alterations as the pneumonic process (reduction of red blood cells and increase of fibrin), so that generally it must from chemical reasons rather increase than diminish dyspnœa.

ON THE HEART.

23-24. The exudation process, the underlying disease itself, is the most probable cause of the increased pulse rate, rather than mechanical obstruction or the reduction of the red cells.

25. The pulse-rate drops after the venesection, but (26) the influence of venesection is usually only transitory and (28) can only occur if the individual is sufficiently full blooded.

31. In the unbled pneumonia there is seldom seen the same amount of cardiac disturbance as in the bled.

The tumultuous heart actions are in part consequences of the venesection.

ON THE PULSE.

The indications for venesection were for the most part determined by the character of the pulse. The quiet, repressed pulse was considered favorable; the large, dicrotic, unfavorable, often seen in severe pneumonias and often bled for. To Dietl's mind the large pulse more regularly followed bleeding; to him it was a sure sign of increased serosity of the blood and asthenia; it was bad if it followed the first bleeding, and, further, he asserts that the return to a small normal pulse from a large dicrotic one was never so quick in the venesected cases as in those treated with dietetic measures alone.

The pulse of the pneumonias is dicrotic, but not completely so as in typhus.

The repressed pulse of the older pathologists is the normal and favorable; the large dicrotic is the abnormal and unfavorable of the various pulses of the pneumonias.

After single or repeated bleedings the pulse becomes large and dicrotic, it becomes "free," as one is accustomed to say; this "becoming free" of the pulse is a sure sign of increased serosity of the blood and asthenia.

It is bad if the pulse becomes free after the first bleeding.

In pneumonia treated by venesection, the large dicrotic pulse never returns so quickly to the normal as it does in those treated with dietetic measures alone.

ON THE JAUNDICE SEEN IN PNEUMONIA.

Bilious pneumonias, our pneumonias with jaundice, were, by Dietl, seen to occur in direct proportion to the extent of the bleeding. Jaundice occurred but seldom in, and quickly disappeared from, the cases not molested with the lancet. On the other hand, it could be seen to deepen after each opening of the vein, and in many instances was directly produced thereby. To instance this:

The yellow color of the skin begins to decrease immediately after the completion of the exudate, and disappears within a very short time.

The yellow color of the skin occurs less often in the unbled cases.

The jaundice increases after each bleeding.

The jaundice is in many cases directly brought about by the bleeding.

It was interesting to note, in connection with the question of jaundice in pneumonia, that the pathologists of Dietl's time had recognized that obstruction of the large ducts and gross liver changes were not usually demonstrable in the fatal cases. To fasten the blame for the jaundice upon the bleeding would be Dietl's natural inclination in such cases, and in the substance of the monograph we find the following:

Venesection promotes excretion of and coagulation of the fibrin to a high degree, and from this comes an abnormal collection of pigment in the blood.

ON THE SPUTUM.

That group of aphorisms which concern the sputum and the effect of bleeding upon its character makes one feel certain that Dietl must have been quite unacquainted with the work of either Laennec or of Louis, or that he willingly ignored both. He still busies himself with the venesection's power to produce the *sputa cocta* in the face of Laennec's clear description of the pneumonic expectoration, and his assault on bleeding is delivered at Andral, quite over Louis' shoulder, as it were: "Andral und andere Beobachtern die die Lanzette stets bei der Hand haben," Two of the aphorisms stand out:

The best pneumonias are those in which there is but little expectoration.

The sputa cocta are not a necessary product nor are they to be considered as a critical evacuation.

To these he adds the following:

It is a very favorable sign and one pointing to a quick resolution, if the expectoration ceases after completion of the exudate.

In the treatment of pneumonia by venesection the sputa undergo several alterations, among which is the transformation of the clear, tenacious expectorations into the so-called sputa cocta.

Venesection favors the breaking down of the pneumonic exudate into pus or pus-like cells, and indeed sputa cocta are often the product of venesection.

As we saw in Aphorism 2, Dietl was fair enough to give credit to bleeding for certain minor qualities; one other of these was its apparent power to relieve cough in the early stages.

Incontestable experience teaches that a single venesection will often lessen a cough or completely subdue it.

The short dry cough of pneumonia is due to the hyperæsthesia of the lungs.

The actual cause of the cough is a bronchitis.

Venesection lessens the cough by subduing the pulmonary hyperæsthesia and by diminishing the bronchial secretion; a similar mode of action is at work in the relieving of the dyspnœa.

Nihilism breaks forth in his declaration, "The expectant treatment has no remedy for the pneumonic cough."

Few of us realize how drastic the treatment of the disease could be before the various protestants had effected their reformation. The convalescence from any serious ailment must have been much prolonged; the critical resurrection of a pneumonia patient must have been often actually interfered with. Laennec realized this to a certain degree. Louis' arguments are always along rather different lines, and he could still see the marked improvement after the vomiting caused by the tartar emetic. Dietl would seem to strike here his highest note. From his aphorisms on this stage of pneumonia we may cite:

After the completed exudation in the unmolested pneumonia, the physiognomy expresses the highest degree of well being.

In the cases treated by bleeding this favorable change of the physiognomy does not show in so striking a manner, because the weakness induced by the bleeding does not leave the patient free to enjoy his return to well being.

In the expectant treatment the appetite returns immediately after the completed exudation; there is seldom craving for heated foods.

In the venesected cases the appetite returns but slowly; there is often a craving for hot food.

In the cases treated by venesection there is much greater wasting than in those treated by dietetic measures.

In the expectantly treated pneumonias the weakness vanishes with the completed exudation and the patient rapidly recovers; in the venesected cases the patient may feel better, but he has yet to go through a long siege of weakness.

The length of convalescence is much shorter in the expectant than in the venesecting treatment.

Dietl realized that bleeding had but little effect upon the lesion. He says in this connection:

Clinical and physiological observations speak for the fact that bleeding has no power to limit the pneumonic exudate.

Venesection even favors the extension of the hepatization.

Many in- and ex-tensive pneumonias occur and flourish under the lancet.

A few more generalized dicta remain; they lead us to a forceful climax.

A pneumonia left to itself is very seldom fatal.

Pneumonia treated by venesection is often fatal in itself.

The expectant treatment of pneumonia shows a much more favorable mortality record.

Venesection has a certain and none too innocent a part in the great mortality of pneumonia.

Venesection kills by increasing the blood disturbance.

Bleeding is not necessary to the re-establishing of health and therefore is not indicated.

Bleeding in many cases *works real harm*, and though no measure may at times give such striking and quick relief, yet the application of bleeding in pneumonia is to be limited to the utmost or, what is safer, is to be thrown completely aside.

THE EARLY DIAGNOSIS OF PULMONARY TUBERCULOSIS.*

By Louis Hamman, M. D.

On the afternoon of the twenty-first of February, 1905, a special meeting of the Laennec Society was held in this amphitheater to open with fitting exercises the Phipps Dispensary. The gifts of Mr. Henry Phipps had made possible the execution of the plan cherished for years by Dr. Osler to have a special department for the study of tuberculosis and the care of tuberculous patients. The old stable facing Monument street had been reconstructed into a two-story building to serve as dispensary and laboratory. On March 1 of the same year the clinic opened to receive patients. The meeting tonight, therefore, is the decennial commemoration of the opening of the Phipps Dispensary for Tuberculosis, and the occasion has for me a deep emotional content, since during these ten years I have been intimately concerned in its fortunes. The years have pased quickly, so quickly that I still feel somewhat the discouragement of the early struggle mingled with the enthusiasm of the period of highest activity and the satisfaction that the department has in the end earned a recognized place in the medical clinic of this hospital. The source of the greatest satisfaction to all of us who have worked in the dispensary is the belief that the attitude we have gradually come to assume towards the diagnosis of pulmonary tuberculosis has colored and perhaps even shaped the attitude that is now accepted by the medical clinic as a whole. It would be a pleasure for me reminiscently to unfold the gradual development of the dispensary; to dwell upon the men who have worked there so faithfully and of their influence upon the work, and to speak of the numerous publications that have come from the clinic and the laboratory. I wish I could describe to you the spirit of kindly and genial good fellowship that has pervaded the staff and has made the work so pleasant and personal contact among the members so delightful. However, dear as these memories are to me, they have not the same force to move you and they deserve no place in a medical discussion. Nor does the time at my disposal allow me to review all of the medical work done in the dispensary. The opportunities offered us have directed our attention particularly towards the diagnosis of pulmonary tuberculosis. I have said that we have come to assume a certain attitude towards this problem, and, since we believe that this attitude sums up the best of our clinical work, I shall content myself with describing it and pointing out its bearing upon some general clinical and sociological questions. In describing the attitude I shall trace briefly the manner in which it has come gradually to be assumed, since I shall thus include justification with definition.

When the dispensary was opened interest in tuberculosis was already running at a high mark. During years of patient and persistent effort the medical profession had gathered small streams of enthusiasm into a large flood which had outrun the profession and was growing deeper and deeper with the inflow of wide-spread social interest. Tuberculosis could be stamped out—so the evidence seemed clearly to indicate—and since the way was there the means to follow it must depend only upon willing disposition and energy. I need not review the program of campaign other than to state that the diagnosis of pulmonary tuberculosis and its cure were essential features. Sanatorium reports gave glowing accounts of the prompt benefits of treatment, while at the same time insisting that these benefits were in direct proportion to the earliness of diagnosis. It was assumed that every case of pulmonary tuberculosis has an early stage; that this early stage can be diagnosed by the skillful; that early diagnosis insures recovery and, therefore, that the solution of the tuberculosis problem depends in large measure upon the diagnostic skill of the medical profession. "Tuberculosis is a preventable and curable disease" was the slogan, and the profession was preached to in and out of season about the necessity of early diagnosis and privately and pub-

* Remarks made at the meeting of the Laennec Society, held February 24, 1915, on the occasion of the decennial of the Phipps Dispensary for Tuberculosis.

licly censured for its deplorable inaptness in this province of medicine. One was surrounded by the conviction that an enlightened profession could quickly save the day and stimulated to hope that by earnest appeal and vigorous pricking the conscience of the profession could be aroused to a sense of its gross deficiency and its heart warmed to yearn for the enlightenment that desire and honest effort would surely bring.

For the moment I shall not stop to separate truth from error in these statements. They are of interest now only to picture the atmosphere in which the dispensary work was begun. We were still young enough to feel the influence of enthusiasm at beginning a new work; to have an ear for the last word of authority; and loyal enough to our profession to feel the sting of opprobrium cast upon it and to resolve that at least in our small way we would by practice and influence contribute to make the rebuke unmerited. Our hearts were, as you see, in the right place regarding early diagnosis, but our skill was scarcely equal to what was demanded of it. This deficiency we sought to correct by assiduous application, and so earnest were our efforts that at the end of a year, or perhaps two years, we could pick out changes in the percussion note and slight alterations in the breath sounds with an agreeable nicety. At the end of that period we were making the diagnosis of pulmonary tuberculosis early enough to content the most exacting sanatorium physician—and that is saying a great deal. Indeed, I know no other way of expressing satisfactorily our interest, our enthusiasm and our finesse in physical diagnosis. In August, 1907, we published a short article on the early diagnosis of pulmonary tuberculosis which I have re-read with interest because it confirms the account I am giving you of our attitude at that early date.[1] The concluding paragraph of the article sums up the situation thus: "In conclusion we desire to express our opinion that in the diagnosis of an early case of pulmonary tuberculosis no abnormality of the physical signs should be disregarded, no matter how unimportant it may be at first sight. A single click, if it persists after coughing and deep breathing, and especially if it is heard at the same spot on subsequent examinations, should put us on our guard and arouse us to use all the means we have to make a correct diagnosis—whose importance is inestimable in these cases. Only in this way will it be possible to diminish the enormous mortality and morbidity which accompany this disease, and which are a disgrace to the medical profession which to-day, more than ever before, is responsible in large measure for the conditions of life resulting from tuberculosis."

This was the period of direct and simple satisfaction in the dispensary work. Slight abnormalities in the physical signs in any person with symptoms enough to bring them to the dispensary were regarded as evidence sufficient to justify a diagnosis of pulmonary tuberculosis and this diagnosis, followed by treatment in a sanatorium, or, in some instances, at home, gave just such gratifying results as were promised to reward enlightenment. However, even at that early day the seed of doubt had been sown and its growth was beginning to trouble our faith in this simple and satisfactory plan. It is difficult to discover the source and observe the early growth of doubt; it generally obtrudes itself full-grown and unexpectedly upon our vision; however, I believe it was the use of tuberculin that first introduced it. In the report of 1907, already referred to, what we had done with the subcutaneous test and the conclusions we were willing to draw from its evidence are briefly considered. To my surprise I find there very clearly pointed out that a failure to react is very strong evidence against the patient having active tuberculosis; that a focal reaction is definite evidence of its presence; that a constitutional reaction is equivocal, since 60 per cent of healthy adults show such a reaction. I am particularly pleased to read the following: "It must be remembered that a patient may have a pulmonary disease other than tuberculosis and still react to tuberculin." "We are willing to admit that, relying upon its (tuberculin's) aid, we may send to the sanatorium some patients who would have recovered perfectly had they continued their accustomed mode of living."

In June, 1908, was published a complete report of our experience with the subcutaneous tuberculin test and a preliminary note upon the cutaneous and conjunctival tests which had been introduced the previous year.[2] During the first year of our work in the dispensary we began using the subcutaneous tuberculin test for diagnosis upon patients at Eudowood Sanatorium and St. Agnes' Hospital and subsequently upon ambulant patients. Of the first thirty patients tested at Eudowood all but one reacted, and we accepted these results as a satisfactory confirmation of our diagnostic criteria. However, a wider application of the test soon robbed us of this satisfaction, because it made apparent that, no matter how trivial the evidence of disease might be, tuberculin almost uniformly confirmed the slightest suspicion and indeed that many individuals with no valid evidence of tuberculous disease also reacted. About this time very enthusiastic reports of the value and importance of tuberculin diagnosis were coming from the German sanatoriums. A tuberculin reaction was given almost equal value in evidence as finding tubercle bacilli in the sputum and such statements as "The patients in this group all had tubercle bacilli in the sputum or else reacted to tuberculin" were frequently made as a guarantee that all the patients undoubtedly had pulmonary tuberculosis. Tuberculin was vaunted as the "sovereign means with which to establish the proper diagnosis with absolute certainty"; and "the quintessence of tuberculin diagnosis" was said to reside "in the Sicherstellung—the making absolutely sure of the diagnosis in doubtful cases."

We took at no time a part in this wave of tuberculin enthusiasm, which retains defenders to the present day. Our experience, together with the welcome statistics of Beck and Franz, ranged us strongly against it. A very conservative attitude is maintained throughout the report of 1908, an attitude the correctness of which subsequent experience has amply confirmed. Indeed, I have nothing of importance to add to what was then said about the subcutaneous tuberculin test and

[1] Hamman and Wolman: The Early Diagnosis of Pulmonary Tuberculosis. Johns Hopkins Hosp. Bull., 1907, XVIII, 299.

[2] Hamman: The Use and the Value of Tuberculin in the Diagnosis of Pulmonary Tuberculosis. Arch. Int. Med., 1908, I, 443.

nothing to retract, except perhaps a little overzealousness in the matter of detecting focal reactions in the lung. The diagnostic importance of a negative tuberculin test and of a focal reaction are duly emphasized and it is as clearly pointed out of what little value is a constitutional reaction alone in establishing a diagnosis of active tuberculous disease.

In May, 1909, and December, 1910, we published two extensive reports upon the cutaneous and conjunctival tuberculin tests [3] and the conclusions then reached are the basis for the interpretation we still place upon these tests. I know with what disfavor the conjunctival test is at present regarded and indeed, influenced by reports that reach me, I am willing to grant that the test should be neither generally nor indiscriminately used. However, I still believe that when proper care is exercised the test may be employed without fear. We have continued to use it in the Phipps Dispensary as a routine procedure and, while very rarely disagreeable reactions occur, I have observed no serious consequences to follow. We surely are beholden to the test for important clinical aid and I think our dispensary clinic would suffer a definite loss should subsequent experience necessitate its abandonment. As you know, we attach considerable value to the 1 per cent conjunctival reaction as confirmatory evidence of the presence of tuberculous disease and, though we have made the attempt repeatedly, we have been unable to draw an equally valuable indication from quantitative cutaneous tests. However, we have always insisted upon the same conservative interpretation of these local tuberculin tests that we have applied to the subcutaneous test, and we have consistently deplored attempts to stretch their meaning beyond the relative limits that critical study justifies.

From 1907 to 1910, the period during which our tuberculin studies were pursued with greatest diligence, a decided change gradually crept into our attitude towards the early diagnosis of pulmonary tuberculosis. There was attack and resistance in the clinic and contention among the staff before our present views were firmly established. As I have said, I think tuberculin was responsible for arousing the suspicion that matters were not so pleasantly simple as we had at first supposed, but suspicion, once aroused, led us quickly to review all the data upon which our conviction rested. This review drew our attention at once to the fact that only a small number of patients with signs of slight pulmonary disease could be sent to the sanatorium and that most of those forced to remain or voluntarily staying at home seemed somehow to be but little injured by the disease. True enough, the physical signs which were the main prop to the diagnosis did not disappear, but, on the other hand, neither did they advance and very few suffered the curse of onrushing disease which we were led to believe would surely follow indifference or neglect of these ominous forebodings. About this same time we were engaged in examining medical students and young women entering the hospital training school and, to our surprise, though they had absolutely no symptoms of disease and were to all appearances in perfect health, still, in a large proportion, we found just such slight pulmonary abnormalities as those upon which, in the clinic, so much emphasis was being laid. Slowly values were readjusted and given what we now consider their true relation. At any rate diagnosis from then on came to mean something more than finesse in percussion and auscultation. At the same period, though of course to a less degree before, the clinic, or perhaps I should say the best men in the clinic, began to show an inquisitive interest in detecting non-tuberculous pulmonary disease masking as tuberculosis. An interesting group of non-tuberculous pulmonary infections was picked out; cases of spontaneous pneumothorax, unresolved pneumonia, empyema, pulmonary infarct, Graves' disease and others were recognized. I mention separately advance in the diagnosis of pulmonary conditions in children, a field in which diagnosis is so difficult, tuberculosis slipping in when least expected and lesions apparently tuberculous not rarely clearing up promptly.

Evidence of this readjustment soon appeared in our publications. In August, 1909,[4] reporting the results of tuberculin treatment among dispensary patients, we recognized the difficulties of early diagnosis and insisted upon establishing a separate group for those in whom the diagnosis could not be made with assurance, labeling this group "probable"; for the same reason a similar classification had been adopted in analysing the results of the conjunctival and cutaneous tuberculin tests. Again the relation of early diagnosis to sanatorium treatment is pertinently referred to in an article on the prevention of tuberculosis that appeared in February, 1910 [5]—and the whole question is briefly considered in a discussion published in the Bulletin for July, 1911.

Up to 1910 we had used the Roentgen-rays in the diagnosis of pulmonary conditions only in special cases presenting unusual physical signs, or as a means of verification in doubtful cases. In the summer of this year Dr. Dunham, with the assistance of Dr. Boardman and Dr. Wolman, undertook to study the value of Roentgen-ray examinations in the diagnosis of pulmonary tuberculosis. A special apparatus was installed to facilitate this study and for four months the work was devotedly pursued. A report of the investigation was published in July, 1911.[6] Bearing upon the question of early diagnosis the study revealed an unexpectedly close agreement between the results of physical and Roentgen-ray examinations. It is true that the roentgenograms showed more extended lesions than would have been anticipated from the physical signs, but the location and, to a less degree, the extent of the changes were for the most part accurately predicted before the pictures were taken. This work, taken in conjunction with many other similar studies, demonstrates with what wonderful pre-

[3] Hamman and Wolman: The Cutaneous and Conjunctival Tuberculin Tests in the Diagnosis of Pulmonary Tuberculosis. Arch. Int. Med., 1909, III, 307; *ibid*, 1910, VI, 690.

[4] Hamman and Wolman: Tuberculin Treatment Among Dispensary Patients. Johns Hopkins Hosp. Bull., 1909, XX, 225.

[5] Hamman: The Prevention of Tuberculosis. Jour. Outdoor Life, 1910, VII, 29.

[6] Dunham, Boardman and Wolman: The Stereoscopic X-ray Examination of the Chest. Johns Hopkins Hosp. Bull., 1911, XXII, 229.

cision changes of density in the lung may be outlined by the Roentgen-ray. Unfortunately, however, Roentgen-ray examinations applied to the early diagnosis of pulmonary tuberculosis suffer all the shortcomings inherent in physical examinations; indeed, they have these short-comings to a still greater degree. Briefly, their inadequacy depends upon this, namely, that, though they give us a precise picture of pulmonary density, nevertheless from this picture we cannot draw either etiological or physiological conclusions. Thus, as regards tuberculosis they do not distinguish active from inactive lesions, which is the important clinical decision. Physical examinations are subject to the same criticism, but they have a decided advantage over Roentgen-ray examinations, in that they discover not only density but moisture as well.

At this time, that is, in 1911, conservatism was the note of the dispensary attitude towards the early diagnosis of pulmonary tuberculosis, and a diagnosis based upon insufficient evidence, especially when slight changes in the physical signs afforded the only evidence, was no longer tolerated. We were gradually getting upon our records valuable data which would in due time decide the practical outcome of the more rigid standards we had set. A study of these records was begun in 1912.[1] For this study a thousand cases were selected, which had some years before been carefully tabulated for the second report upon the conjunctival and cutaneous tests. The later history of these patients was sought by personal interview and letter and satisfactory data concerning 632 were obtained. In the present connection we are interested only in the doubtful group of cases comprising 258 of the patients. Had the analysis shown that a large number of doubtful cases had subsequently become tuberculous, then our conservatism would have been condemned and banished. However, far from showing anything of that sort, the analysis has furnished the very strongest support to our conservatism. Of the 258 patients reported upon, 176 were well; 57 unimproved, that is, the symptoms that had brought them to the dispensary still persisted; 16 had become frankly tuberculous; 9 had died of some cause other than tuberculosis. I must refer you to the report for a closer study of the interesting figures, for, although 6 per cent of the patients became tuberculous, a relatively large number, still the character of these 16 cases will give you a better notion of how much emphasis the figure merits.

There is only one more study to mention and the notice will be brief.[2] I have said that in making routine physical examinations of a large number of students and nurses our attention was early drawn to the frequent occurrence of more or less marked apical abnormalities in perfectly healthy adults. To put this experience in precise form, we studied with unusual care the pulmonary physical signs in fifty healthy students and controlled the physical findings with roentgenograms. As we anticipated, a large number showed definite abnormalities on physical examination, abnormalities that were confirmed by the Roentgen-ray findings. The roentgenograms are particularly instructive in calling attention to the extensive changes present in the lungs of healthy adults about whom hovers no suspicion of active pulmonary disease. There are some who now consider the Roentgen-ray "the sovereign means with which to establish the proper diagnosis with absolute certainty" in early pulmonary tuberculosis, just as others hold tuberculin to be this regal means. I believe studies similar to the one we have made will have a sobering influence upon their enthusiasm.

You must see now to just what point our ten years' study of the early diagnosis of pulmonary tuberculosis has brought us. Not the anamnesis, nor the physical examination, nor tuberculin, nor the Roentgen-ray, nor any other means with which we are familiar, taken alone, is adequate in the making of a decision in this momentous question. Diagnosis here, as in nearly all other fields of internal medicine, is reached through skill, judgment, and experience; skill in the application of methods; judgment to carefully weigh the results, and experience to give them the proper interpretation. While exploration of the lungs is, in my opinion, the most difficult domain of physical diagnosis, still I would insist that the early diagnosis of pulmonary tuberculosis rest upon many pillars and not be supported alone by finesse in percussion and auscultation.

Throughout these remarks I have spoken of "slight abnormalities in the pulmonary physical signs" and have been rather severe in my criticism of what I consider the undue importance that has been attached to them in early diagnosis. It remains for me to make perfectly clear, if I am able to do so, just what is meant by "slight abnormalities." In relation to physical diagnosis, the medical profession may be divided into the skillful and the unskillful. I am forced to say, from my own experience, that the vastly larger number is unskillful. I hasten to add that the judgment is passed in no spirit of criticism or censure, for proficiency in the arts of pulmonary auscultation and percussion is reached and maintained only by close and persistent application; an attention which most practitioners have neither the time to give nor sufficient motive to cultivate. To the group of physicians to whom even relatively gross lesions are a source of difficulty and uncertainty in diagnosis, I have at present nothing to say. I have elsewhere expressed the opinion that much more will be accomplished by encouraging them to observe closely and critically the general symptoms of the disease than by insisting upon skillful examinations. It should be urged particularly that when obvious symptoms are present their importance be not subverted by a so-called negative examination.

The physicians skillful in physical diagnosis may be subdivided into those more and those less skillful; the more skillful being represented in the main by sanatorium physicians and those particularly interested in tuberculosis, the less skillful by those engaged in the general field of internal medicine who, nevertheless, on account of the prominent position occupied by

[1] **Gellen and Hamman: The Subsequent History of One Thousand Patients Who Received Tuberculin Tests. Johns Hopkins Hosp. Bull., 1913, XXIV, 180.**

[2] **Hamman and Baetjer: Pulmonary Physical Signs and Roentgen-ray Findings in Healthy Adults. Arch. Int. Med., 1914, XIV, 757.**

pulmonary disease in this field, are made daily to practise and display their skill in percussion and auscultation. The former group, on account of specialized training, has the greater skill, but I believe it has allowed virtuosity somewhat to obscure its judgment; the latter group, on account of wide experience, has the better judgment, but I believe it has allowed wide interest somewhat to dull the practice of its art. Both groups, however, will appreciate the bearing of my remarks and sympathize with my difficulties.

To return now to the definition of slight abnormalities in the pulmonary physical signs. By these I mean slight differences between the two sides of the chest on inspection; slight changes in the percussion note, situated practically always at the apices; slight changes in the intensity and quality of the breath and voice sounds, also nearly always at the apices. Any obscurity in this definition resides in the word "slight" and it was in preparation for this difficulty that I arbitrarily grouped the profession into the skillful and the unskillful as regards physical diagnosis. Had I the gift, which I have not, of the most penetrating lucidity of expression, I could not clear away this difficulty for the unskillful, whereas the skillful will appreciate its meaning without further ado. In comparing the value of physical signs with Roentgen-ray findings in pulmonary diagnosis I have already said that the former has an immeasurable advantage, in that it detects moisture as well as difference of density, and I will conclude my remarks on this aspect of the subject with a few words about the significance of râles. Let me add that by râles I mean the definite moist sounds that are heard at the apices at the end of inspiration and commonly enough only after cough; and that I do not mean the various transient clicks and so-called adventitious sounds that may simulate râles so closely and often puzzle the adept and mislead the novice. Allow me further to qualify what I am about to say by adding that I refer to localized râles found when all the other clinical features of the case in question make a diagnosis of pulmonary tuberculosis not only reasonable but probable. For instance, râles, even at an apex, would have quite a different significance if the symptoms and other physical findings pointed frankly to the diagnosis of lobar pneumonia. These restrictions being clearly understood, I am prepared to state upon wide experience that when localized râles are discovered in the presence of symptoms and other physical signs pointing towards pulmonary tuberculosis, the diagnosis is practically assured; and by diagnosis I mean a clinical, not an anatomical, diagnosis; or, in other words, that the patient has an active tuberculous lesion. The discovery of râles, thus restricted, I place second only to the finding of tubercle bacilli in the sputum in the diagnosis of pulmonary tuberculosis. Alas! when we possess the assurance that râles give us, for the sanatorium physician the patient has already passed out of the class favorable for treatment.

In concluding, I return to the tenets that comprised our faith at the opening of the dispensary to see how these have fared in the light of more mature experience. You will remember that we were guided by the belief that every case of pulmonary tuberculosis has an early stage, that this early stage can be diagnosed by the skillful, that early diagnosis insures recovery and, therefore, that the solution of the tuberculosis problem resides to a large measure in the diagnostic skill of the medical profession. How have we departed from the simple faith of our childhood and how scepticism and dissent have corroded this creed! The very first premise—that every case of pulmonary tuberculosis has an early stage—is tinged with gross error. Tuberculosis is not an infection that always begins as a minute lesion in the lung, from which lesion the disease gradually and slowly spreads to neighboring areas, giving at first but indefinite signs of its presence and only later causing obvious symptoms. Rather, it commonly strikes abruptly and unexpectedly; it pounces upon an individual in full health and then continues, as it began, not with slow progression, but by leaps and bounds. A large number of cases of pulmonary tuberculosis have no early stage, but jump at once from health to a moderately advanced or advanced stage of the disease. Thus a man starts out in the morning upon his affairs in his usual good health; in the afternoon he feels draggy and feverish; he keeps to his bed, runs a fever and begins to cough; little is found immediately upon examination, but two weeks later half a lobe or a whole lobe is involved; another has hemoptysis, followed by a similar course of events; still another begins with "grip" and though not ill enough to remain in bed still can name the very day upon which the illness began. I repeat, clinically the disease as commonly begins in some such abrupt manner as in the slow, creeping fashion that propagandists delight to picture. Were it not so, then why is it that early cases of pulmonary tuberculosis so persistently elude us? We see very few cases of incipient tuberculosis in the dispensary and we have a large and varied material to draw from, an unusually favorable material from which to pick out early cases. If you say that our standards of diagnosis are too rigid, then I point to our results for justification; if you say that patients do not present themselves for examination early enough, then I reply that we have examined large numbers of exposed individuals and have failed to find early tuberculosis. If it were possible to have all the inhabitants of Baltimore submitted to ever so rigid a clinical investigation, I firmly believe that it would be impossible to pick out those who will be frankly tuberculous at the end of a month. Once having taken our present stand on the early diagnosis of pulmonary tuberculosis, few cases that are definitely tuberculous will fall into the incipient group. The reason for this I believe resides more in the nature of the disease than in lack of diagnostic ability.

The second premise—that the early stage can be diagnosed by the skillful—I need mention only briefly. What has just been said robs it at once of half its importance. Concerning the other half I would remark that the necessary skill will never be the common possession of the profession as a whole. We have no more right to demand of it exceptional training in this field than in any other special field of medicine and to master them all is quite impossible.

That early diagnosis insures recovery is in a measure true and if we change "insures recovery" to "makes recovery likely" we are still nearer the truth. What I have said of the difficul-

ties of early diagnosis offers an explanation for the very small number of cases of incipient tuberculosis that we find in sanatoriums. I say in sanatoriums, because it is there that we would naturally expect to find them and because it is there that we look also for a demonstration of the effectiveness of treatment. In sanatoriums there are two classes of cases: the definitely tuberculous and the questionably tuberculous. How many of the former, how many of the latter, will depend somewhat upon the questioner. As definitely tuberculous we may include those with tubercle bacilli in the sputum and those with frank signs of pulmonary involvement, meaning by frank signs impairment of the percussion note, change in the breath sounds and moist râles. Although a few of the patients showing such frank signs will upon careful investigation prove to have non-tuberculous pulmonary affections, this number will be too small to introduce a serious error. In this definitely tuberculous group the results of treatment depend largely upon intelligent co-operation and the financial possibility to co-operate. Thus among the intelligent with a reasonable income the results will be good, whereas among the poor the results will be most discouraging. Unfortunately, tuberculosis is prevalent chiefly among the poor and the results obtained at state sanatoriums with this class of definitely tuberculous patients have been very disappointing. Temporary improvement is usually followed by prompt relapse when the patients return home to their unsatisfactory living conditions. The questionably tuberculous group includes those patients without the specific clinical marks of tuberculous disease. Many of them have symptoms strongly suggestive of the disease without definite physical signs; others have both indefinite symptoms and signs. While there can be little doubt about the diagnosis in some of these patients, still in a large number the diagnosis rests in a measure upon individual opinion, a very hazardous prop for cogent conclusions. It is in this group that treatment brings about such brilliant results, results which without warrant have been transferred to the treatment of pulmonary tuberculosis as a whole and have led to exaggerated notions of the curability of the disease.

Having taken exception to all the premises, it is needless to add that we no longer have faith in the conclusion that the solution of the tuberculosis problem resides to a large measure in the diagnostic skill of the medical profession. Were it possible—though we think it is not—to train the profession to a high standard of diagnostic skill, still the nature of the infection and the difficulties encountered in early diagnosis, even by the expert, would be an insuperable barrier to such skill becoming an effective weapon in the campaign against tuberculosis.

To those of us who have worked in the dispensary since its first years this gradual change in attitude towards early diagnosis has been a stimulating source of interest. The change has come unsought, indeed in a way unwelcomed, for it has shattered agreeable delusions and robbed us of fond hopes. We would have been better pleased had our early impressions been confirmed, and as the evidence we slowly amassed pulled us from our first position, we followed unwillingly the path to which it led. The point at which we have arrived is not the satisfactory resting-place we expected to find when we began the journey. Nor do the prospects that confront us justify the cheer of anticipating a speedy deliverance from our difficulties. However, we still have faith and we hope that in the end some way will be found to separate from the large group of doubtful cases that smaller group in whom mild symptoms and slight abnormalities in the physical signs presage the onset of more serious clinical manifestations. If we can ever distinguish clinically that nice point where latent infection first passes into threatening activity, the problem of early diagnosis will be solved. At the present time this point is blankly obscure and we have no means of deciding definitely which doubtful cases are within safety, which have just passed without, and which are hovering about the threshold. Hence it results that early diagnosis is so largely a matter of personal judgment, that it has no fast and sure rules to guide it and that at present there is such a wide difference of opinion within the profession as to what shall be included in the group of early pulmonary tuberculosis. I hope I have made clear to just what attitude towards this important question ten years of sincere and earnest work has brought the Phipps Dispensary.

DISCUSSION.

DR. HUBD: I should like to make an inquiry. What would Dr. Hamman advise us to do for these cases? If it is impossible to find out what is the matter with them, what is the practical application? Shall we keep up our sanatoria and dispensaries, or shall we let them all go? Have we made any progress?

DR. JANEWAY: Perhaps I may be pardoned for saying a few words about Dr. Hamman's paper, as it gives perhaps the only aspect of this subject about which I know enough to have any reasonable right to an opinion. I have been in the position for a number of years of having to arrive at these judgments of which Dr. Hamman speaks and I am in complete accord with his point of view. We are at present face to face with hard facts, and though perhaps the whole blame for the failure to solve the problem of tuberculosis in a short time is not to be borne by the medical profession, nevertheless, it is clear that the lead must come from the medical profession and it is incumbent on us to face the facts and to make a fresh start.

It seems to me that the discussion of the early diagnosis of tuberculosis is more or less academic, with our knowledge of the dissemination of tuberculosis throughout the community and the early age at which infection in a large proportion of the cases takes place. We have to distinguish at once, of course, between the diagnosis of tuberculous infection and the diagnosis of tuberculous disease; but I am inclined to think we have to go further and that what we can aim at practically is perhaps a diagnosis for purposes of prognosis and treatment rather than absolute diagnosis in itself. In order to arrive at that, we must take into consideration other features of the case than those which bear only on diagnosis—in particular such matters as family history and the well-known age and sex factors which enter into the prognosis of the disease; because after all we are aiming at a diagnosis which will determine our advice to the patient. Shall we or shall we not send such a patient to a sanatorium? Shall we, with a patient known to have early and perhaps slightly active tuberculous disease, risk a period of observation at home in order not to inflict a serious economic or personal hardship upon the patient. Those are the difficult ques-

tions which come to us to be solved, and the mere making of the diagnosis does not solve them. We have to individualize absolutely. It is quite clear to me that while physical diagnosis has, as Dr. Hamman pointed out, very striking limitations, and while it is clearly incumbent upon the student above all things to learn the limitations of the methods with which he works, on the other hand, for the bulk of you who are here this evening, the acquisition of such extraordinary acuteness in diagnosis that you find much in the chest that is not there, is not a particular danger. For the next ten years of your lives, practice in the refinement of physical diagnosis will not work much harm to your patients. At the end of that time, you will undoubtedly come to the conclusions Dr. Hamman has reached.

There are a few factors which enter into the early diagnosis of tuberculous disease, however, on which it is desirable to lay emphasis. One of those, in my opinion, is the significance of hæmoptysis. I have seen, in the course of my experience, so many patients who were told that a little hæmoptysis was a bleeding from the throat and of no significance, that it has made a very strong impression. There is no symptom of tuberculosis which helps more in securing the co-operation of the patient in measures which you recommend than hæmoptysis. A patient who has once seen blood will do almost anything you tell him, if you catch him early. My experience, and the experience of my father before me, which was very definite in that regard, has been that patients with hæmoptysis have on the average a better prognosis than almost any others, partly because of the co-operation which you get from them.

The other feature, I think, is the existence of localized fine râles. Though, of course, râles are not an early physical sign, they are sometimes the earliest decided physical signs detected. I have seen patients in whom râles, in spite of repeated examinations, were really the only physical signs I could be sure of, go ahead to complete recovery, although they had bacilli over considerable periods. I remember one instance of this in New York City; a man who continued to pursue his occupation of traveling locksmith and who was perfectly well ten years afterwards, although I had found tubercle bacilli for six months and râles at the apex.

The question of diagnosis must be approached from another standpoint also. One must bear in mind not only what combination of symptoms and signs is highly suspicious of active tuberculosis, but in addition the other possible diseased conditions which may produce the same combination of symptoms and signs. For a number of years I have had to go occasionally in consultation to the Loomis Sanatorium, where I was a member of the medical board, practically always to solve diagnostic problems in regard to some patient sent in for pulmonary tuberculosis, who, after remaining there for from three to six months, could not be proved to have had it. The condition which most frequently caused these errors in diagnosis was perhaps first of all chronic infective endocarditis (streptococcus viridans). I have seen a number of patients who, because of the existence in the lung of evidence of focal broncho-pneumonia with low fever and loss of strength, were said to have pulmonary tuberculosis, the significance of the occasional eruption of petechial spots having been overlooked. Then again there is Hodgkin's disease, with relapsing fever. The differential diagnosis is extraordinarily difficult at times. Or, certain cases of hypernephroma with lung metastases, and a few of the rare primary tumors of the lung, where the distressing cough and loss of flesh, with lung signs lead to the diagnosis of tuberculosis. Lastly comes tertiary syphilis with fever. Then, of course, there is one standing reproach, which comes up in every hospital and tuberculosis dispensary—the appearance of the patient with an old mitral stenosis with recurrent hæmoptyses and recurring attacks of bronchitis, who is sent off to die of tuberculosis. These patients are rarely supposed to be early cases.

I think you ought to bear the above conditions in mind and in approaching any diagnostic problem do so from the two sides: First, the positive evidences of the condition one must suspect; and second, what other conditions might account for the existing symptoms. Then, arrive at a diagnosis by exclusion.

The importance of all this is because the treatment of this disease involves very serious economic and personal hardships and one ought not to require of any patient who can just make his living and keep his head above water, a long standing residence in a sanatorium if he has not the disease for which the sanatorium does good. In dealing with the well-to-do, the attitude of mind can be the opposite, and one can very wisely tell the patient, or the family, that while positive diagnosis is impossible, the present is the favorable time to act.

One other thing to be emphasized is the significance of a previous pleurisy with effusion. Where that is known to have occurred, one ought usually to assume the probable existence of pulmonary tuberculosis on the development of subsequent symptoms and signs.

DR. HAMMAN: In approaching such a large subject as the "Early Diagnosis of Pulmonary Tuberculosis" it is necessary to view the field from a single standpoint. I wish to call attention particularly to the fact that my remarks concerned the early diagnosis of pulmonary tuberculosis only from a broad, sociological standpoint, and not from the standpoint of early diagnosis as concerns the individual patient. In regard to the latter standpoint, I can add little to what Dr. Janeway has said. I am sure that no one could be more eager to make an early diagnosis than I am and I realize fully that the mistakes of the profession are more on the side of hesitating to make a diagnosis, when the conditions fully warrant it, than in making a diagnosis prematurely. As concerns the individual, treatment, which is the ultimate object of diagnosis, depends upon many factors other than strictly medical data. The position of the patient, the amount of leisure at his disposal, his financial condition and business obligations must all be taken into consideration. I have no quarrel with the physicians who treat doubtful cases of pulmonary tuberculosis. Indeed, in many instances I think such treatment is desirable. What I do quarrel with is the tendency which obtains in some quarters to treat these cases as definite instances of pulmonary tuberculosis and to add them to the list of sanatorium cures.

In reply to Dr. Hurd, I would say that to my mind all of the work that has been done has by no means been wasted. I regret very much that my remarks have left the impression that I look upon the situation in a pessimistic way. I believe, indeed, that a great deal of good has been accomplished, but I am thoroughly convinced that the early diagnosis of pulmonary tuberculosis will not play an important part in eradicating tuberculosis as a disease of the masses.

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RESULTS OBTAINED FROM THE INDUCED PNEUMOTHORAX TREATMENT OF PULMONARY TUBERCULOSIS: A BRIEF REPORT.*

By MARTIN F. SLOAN, M. D.

Three years ago Hamman and Sloan presented before this society a report covering a series of 20 cases of chronic pulmonary disease treated by the induced pneumothorax method. To-night they wish to add 23 cases to their series and present in a brief way the results that have been obtained.

It probably seems strange that, with such a large number as have been seen at the Phipps Dispensary to select from, comparatively few patients have been given the benefit of this treatment, but with a clearer understanding of the pertinent points of the procedure the explanation becomes apparent. The whole subject may be discussed conveniently under the four following headings: selection of patients; technique of the inflation; subsequent inflations; duration of collapse.

Selection of cases.—Three years ago the observation was made that, while induced pneumothorax would be of inestimable benefit to a number of cases, it would never become a routine treatment of chronic pulmonary disease, especially tuberculosis. This observation is confirmed by the broadened experience of three years and a judgment matured by a larger number of patients subjected to the treatment. The author selects as suitable for the method patients showing:

(a) Gross and active lesions in one lung, with a quiescent lesion not extending below the level of the fourth rib in the other lung;

(b) Gross and active lesions in one lung, with a mildly active lesion not extending below the level of the third rib in the other;

(c) Quiescent lesions, bilateral but suitably located, with a history of aggravating cough and profuse expectoration;

(d) Arrested lesions, but with a history of recurring hemorrhages;

(e) Arrested, but suitably located lesions, with a previous history of relapse whenever work was attempted.

Patients with incipient lesions have been considered unsuitable, except in cases of hemorrhage, as it was felt that the general natural therapeutic measures should be thoroughly tried before recourse to a radical treatment was made. All the patients treated had moderately or far advanced pulmonary tuberculosis, except one, who had bronchiectasis.

Those designated as unsuitable were patients showing:

(a) Gross and active lesions extending below the level of the third rib on both sides;

(b) An extensive gross lesion in one lung and a lesion located at the base in the other;

(c) Serious complications, such as cardiac disease, arteriosclerosis, ulcerative laryngitis, chronic diarrhoea, extensive tuberculous ostitis and nephritis, either acute or chronic;

(d) Disease apparently of long standing, as shown by marked fibrosis of the lungs, thoracic deformities, decided cardiac displacement and dyspnea;

(e) A history of chronic alcoholism;

(f) A history of recurring hemorrhage from both lungs;

(g) A marked emphysema;

(h) An erratic and excitable temperament;

(i) Real or apparent old age.

Technique.—The technique was that developed by Professor Forlanini, of Pavia. Three patients of this series were first subjected to the Brauer method, but the results did not justify the continuation of such a painful and prolonged technique. As a matter of convenience to the operator and comfort to the patient the Forlanini method has proved to be the more practical. A full description of this technique may be found in the BULLETIN of February, 1913, to which the reader is referred.

Subsequent inflations.—Compression of the lung was induced slowly, giving the other lung and the heart time to readjust themselves. For the initial inflation 500 cc. of gas is sufficient. No absolute rule can be laid down governing the amount to be given or the length of intermissions between subsequent inflations. One is guided by the terminal pressures of the preceding inflation, the estimated amount of gas absorbed since the last inflation, the pulse rate and temperature curve, the effect on weight, cough and expectoration, the patient's general feeling, and particularly by the condition of the working lung. The patients of this series have received, as a rule, 700 cc. of gas at the first inflation, which was followed by a like amount every three days until three inflations had been given. Every two to three weeks thereafter from 500 to 800 cc. were injected. Experience has shown that the smaller amounts of gas frequently administered produce better results than the larger amounts given at longer intervals. When the object of the treatment is to check pulmonary hemorrhage, it is desirable to exert pressure against the bleeding points as quickly as possible, and in such cases as much as 1000 cc. has been given during the initial inflation. The presence of pleural adhesions will upset any previous thought-out plans.

Duration of collapse.—It is exceedingly doubtful if healing sufficient to withstand the resumed functional activity of the treated lung can occur in a shorter time than two years. In Case III of this series the lung, which had been completely collapsed for a year, was permitted to re-expand at the end of that time. Four months after expansion had become complete and functional activity had been resumed, signs and symptoms of activity re-appeared. Nine attempts were made in different places, but nowhere was it found possible to introduce the gas. The pleural surfaces had adhered apparently throughout the entire side. This same experience

* Read before the Laennec Society, February 24, 1915, on the occasion of the decennial of the Phipps Dispensary for Tuberculosis.

was encountered subsequently in two other cases. In the absence of contra-indicating symptoms, such as shortness of breath and persistent loss of weight, there is no reason why compression should not be continued indefinitely, if the working lung is holding up well and the patient is not uncomfortable or inconvenienced.

Briefly, the results in this series of 43 patients treated are grouped as follows:

Special indications for relief.—Case III was having repeated small hemoptyses. There was no recurrence as long as compression was maintained, which was for 16 months.

Case V had a pleural effusion. The effusion was removed and nitrogen introduced.

Case IX had had several frank hemorrhages and was having repeated hemoptyses at the time of the first inflation. Before compression became complete she had several more. She has had none since March, 1912.

Case XI gave a history of frank hemorrhages to within two weeks of the initial inflation; there was no recurrence to the time of death 26 months later.

Case XII was developing a cavity in the upper lobe of the right lung and was having small hemoptyses therefrom. There was no recurrence after compression.

Case XIII gave a history of several large hemorrhages with repeated small hemoptyses up to the time of the first inflation; there has been no recurrence to date, three years and three months after.

Case XVI was having profuse hemorrhages at the time of the first inflation; there was a small hemoptysis 12 hours later. There was no recurrence until eight months later, when hemorrhage started again from the treated lung in spite of an almost complete collapse.

Case XIX was having repeated hemoptyses prior to and at the time of the first inflation. There has been no repetition to date, two and a half years later.

Case XX gave a history of repeated hemoptyses. There was relief for over a year, after which bleeding started from the "opposite" lung.

Case XXI, one of bronchiectasis, gave a history of repeated hemorrhages from the right lung. There was relief for three months following the first inflation, after which bleeding started from the left lung.

Case XXII gave a history of repeated attacks of pleurisy on the right side with sharp pain. The pain was relieved for over a year by partial collapse of the lung.

Case XXX gave a history of repeated hemoptyses. There had been no repetition after 20 months' treatment.

Case XXXII gave a history of profuse hemorrhage prior to the first inflation. There had been no repetition after 18 months of treatment.

Case XXXIII was developing a cavity in the upper lobe of the right lung. There has been perfect health for the past year.

Case XLIII gave a history of repeated hemoptyses. There has been no recurrence since the first inflation over three months ago.

Cases not specified in this group were treated for progression of the disease.

Accidents and Early Death.—Case I developed a pleural effusion which, more than a year after the inflations had been discontinued, became purulent. The pleural cavity was drained through an intercostal space. The wound healed and the patient has been doing splendidly for the past two years.

Case X developed meningitis after the third injection and died 14 days later.

Case XVIII was in a desperate condition when treatment was started and died ten days after the first inflation.

Cases XI, XII, XIII and XXXIII developed a hydrothorax. The fluid became purulent in Case XI a year and a half after the last inflation and the patient died two months later. In Case XII, pyothorax developed three months after the last inflation, from which the patient subsequently died. Cases XIII and XXXIII have been enjoying perfect health for three years and for nine months, respectively, after the development of fluid. A slight amount of fluid persists in each case.

Case V had extensive pulmonary tuberculosis and a pleural effusion. The effusion was partly removed and sterile air injected. The fluid became purulent after the third inflation. Resection and drainage were instituted, but the patient died three and a half months later.

No collapse produced.—Adhesions were so extensive and dense in five cases that it was impossible to inject the smallest amount of gas. The Brauer method was tried in Case VI without satisfactory results. Punctures were made in all available areas of the hemothorax without finding a patent pleural space.

Partial collapse produced.—Owing to adhesions only a partial collapse was produced in 15 cases. The partial collapse existed in various places, the base being held firmly to the chest wall as frequently as the apex. Those in whom only a partial collapse was produced seemed to experience as much symptomatic relief as those in whom a complete collapse was obtained.

Complete collapse produced.—A free pleural space was found and a complete collapse obtained in 17 cases. In several of these it was found advisable to maintain only a partial collapse in the course of treatment owing to a flexible mediastinum, permitting encroachment on the working lung, and to a cardiac displacement.

Of 43 patients treated from three months to three and a half years 18, or 41+ per cent, have died, and 25, or 58+ per cent, are living. Of these 25 living, 8, or 19+ per cent of the whole, are doing poorly; 11, or 26+per cent, are doing well and are working part time. Some of these are inclined to resume their former full working time, but refrain from doing so on medical advice. Six, or 14+per cent, have resumed all of their former business and social obligations. Five of these have been working for over two and one-half years.

The induced pneumothorax treatment applied to the 42 patients with moderately or far advanced pulmonary tuberculosis and one with bronchiectasis, and in whom the prognosis was bad, influenced the progressing course of the disease little or none at all in 60 per cent. That it did, however, stop dis-

tressing symptoms in a large number of these is shown by a careful inspection of the individual charts. That it has given to 11 per cent perfect health and complete working capacity for over two and one-half years certainly justifies the use of the method and establishes it as a valuable addition to our therapeutic armamentarium.

DISCUSSION.

Dr. Wolman: Sometimes in desperation people rush in, perhaps foolishly, where angels would fear to go. I say this in connection with the cautions Dr. Sloan has laid down in administering pneumothorax. He insisted that the better lung ought to be perfectly good. I can recall two cases which have led me to be a little more optimistic than those pessimists associated with me. One sometimes has the feeling in the presence of a dying person that it might be well to undertake even measures that everyone has said will do no good. We happened to have a girl at Reisterstown who attracted everyone by the sunniness of her disposition. She was very sick with a high fever, rest in bed for a long time having had no effect upon her symptoms. We had thought of pneumothorax, but decided it was contra-indicated, because it was hard to tell which was the better lung. However, in desperation we thought we might try it. The result was most beneficial, the fever dropping almost spontaneously. Of course the girl may not be cured, but she has every chance of gaining a few years of comfortable life. It is said that another contra-indication is tuberculous laryngitis. Unfortunately, this girl had that, too. However, the laryngeal lesion improved also. I do not say this to cast doubt on Dr. Sloan's injunctions, but simply because it seems to me that there are some cases in which it can do no harm to try the treatment and in which the patient may receive much benefit.

The second case was that of a man with a bilateral lesion, who had been in bed for about a year, with fever, and who had diabetes also. We were afraid to try pneumothorax on account of the diabetes, so we sent him to the Sanatorium. Dr. Cullen sent him back, however, in a few weeks, saying he ought to die with his family. In this case nature attempted what mortals were afraid to do, and he evolved a spontaneous pneumothorax. The man almost died, but after the first week he improved and the fever which had been running for a year disappeared. These cases would seem to show that some cases with apparent contra-indications will perhaps be benefited by this form of treatment.

Dr. Hamman: I should like to emphasize just one point in regard to the patients Dr. Sloan has exhibited, namely, the advanced stage in which the disease existed in these patients when treatment was begun. I remember particularly the robust young man who was seated in the center. He was quite ill when the treatment was begun, nearly three years ago. He had had a number of severe hemorrhages and had at the time considerable fever and was markedly prostrated. We were just beginning to induce pneumothorax at that time and I think he was given too much air at the first few operations. He failed to improve satisfactorily until he developed an abundant effusion on the right side. Following the development of this effusion he improved in a remarkable way and during the past year has worked actively as an insurance solicitor and has remained in very good condition as you could easily see. The effusion has persisted and his right lung remains completely collapsed. In about one-third of the cases in which we have succeeded in inducing pneumothorax such similar effusions have developed and in these patients it is practically certain that the functional capacity of the lung will be permanently lost. This tendency towards the development of massive effusion makes the treatment undesirable in the early stages of pulmonary tuberculosis. Since, roughly speaking, one-third of these cases will permanently lose the function of the lung, it would be inadvisable to use the treatment until the effects of the ordinary hygienic and dietetic measures had been thoroughly tried out. Of course it is equally important not to delay the treatment too long and if under favorable conditions such early or moderately advanced cases fail to improve, if the conditions are otherwise favorable, pneumothorax should be employed.

Dr. Sloan: I feel in beginning a new and radical treatment like this one we should do so in a conservative manner. Up to the present time we have been more or less conservative in selecting our candidates; in fact, during the last two years we have inclined more and more to conservatism. Dr. Wolman is evidently going through the same period we went through in our early experiences with the process. I believe in the future the tendency will be to select earlier cases for treatment when, especially after observation, it is seen that under the ordinary treatment the patients are likely to do badly.

I think we are entirely justified in selecting the early cases whose histories show a breakdown on any attempt to resume their occupations.

In regard to what Dr. Hamman says about effusions, it is true that a good many of the patients develop an effusion, but in our last 12 patients with complete collapse we have not had a single one. It is difficult to account for the development of this complication. We thought at first it was due to obstruction of the circulation in the pulmonary lymphatics, but in some cases the effusion did not develop until the most favorable condition for this complication—the period of complete collapse—had passed and the lung had almost re-expanded and resumed its function. Neither does it seem to be due to trauma, such as occurs when adhesions are stretched; yet it does appear occasionally at this time.

A BRIEF EPITOME OF THE RESULTS OF SANATORIUM TREATMENT.*

By S. Wolman and I. I. Hirschman.

It is natural that the sanatorium should view with greater optimism the results of sanatorium treatment than the dispensary, which sees the discharged patients after they have returned to their homes in the city and have attempted to reenter the economic life.

Our general impression, built upon what we saw in the daily routine of the Phipps Dispensary, was that the results of treatment were frequently disappointing. In order to test the validity of our impressions, we studied the list of admissions to the State Sanatorium since its opening, and without any selection whatever identified as many as possible of those patients that had been examined at the Phipps Dispensary. We included also in this study a comparatively small number of patients who had been at local sanatoria other than the State Sanatorium.

We examined the histories of 403 patients who had had the advantages of sanatorium treatment. Of these, 262 had to be

* Remarks before the Laennec Society, February 24, 1915, on the occasion of the decennial of the Phipps Dispensary for Tuberculosis.

discarded, because 132 were still in the sanatorium, and concerning 130 we had no data as to the result after discharge. There remained 141 patients of whose subsequent fate we had knowledge. Of these 141 the dead number 51, the living number 90. Of the 90 living, 44 are worse, 16 not definitely worse, 30 are better than when we first saw them.

That is, out of 141 cases, only 30 are improved and 111 are dead, worse, or not improved. Of the 39 apparently better, 4 had tubercle bacilli in the sputum. Of the 111, 47 had tubercle bacilli in the sputum.

It would not be reasonable to assume that all of the 130 patients concerning whom we had no data should be numbered with the improved. Should this unreasonable assumption be made, we would have 111 dead and worse, against 160 better. The results are all the more distressing when we consider that the period since discharge from the sanatorium has not been at all long.

Our conclusions derived from the observation of the patients in our clinic, are that in great part the cause of this poor showing lies in the premature dismissal of patients, especially when these belong to the poorer classes. We recommend a one or two years' residence for early cases, an indefinite stay for active cases, and the privilege of readmission for relapsed cases. We are especially opposed to any predetermined routine of length of residence, and urge an individualization. No patient should be discharged until he seems able to make a living for himself and family without danger of relapse.

DISCUSSION.

Dr. Henry Barton Jacobs: It would be very unfortunate if this large group of students were to go away from here to-night thinking that the problem of tuberculosis from a social standpoint was not progressing. It certainly is. The best statistics we can gather are from Massachusetts, New York and Pennsylvania, and in these states in the ten years since the dispensary opened the mortality from tuberculosis shows distinctly a fall of from 40 to 50 per cent. What factors have brought this about may be open to question, but that tuberculosis is on the decline there can be no doubt.

The whole tuberculosis movement has been an hygienic movement. Rural living, suburban residence, the extension of trolleys into the country, all have come about largely since the tuberculosis problem has been under discussion. The desire for better housing, cleaner streets and better sewerage all goes hand in hand with the tuberculosis movement. To what extent the direct attack upon tuberculosis itself is responsible for the fall in the death rate, one perhaps cannot determine, but, as I say, the whole hygienic movement seems to be more or less dependent upon the incentive it originally received from the idea that tuberculosis can be cured if it be given a chance. If then this be the result of the crusade against tuberculosis, that the death rate in the best communities has been halved, certainly we should take courage to continue the fight.

The question of the number of cures in sanatoria or hospitals is one I have studied for a good many years. The more we learn about the cases discharged, the more we are inclined to believe in figures such as Dr. Wolman has presented. Still while only 30 saved out of 300 may seem to be poor results, probably these 30 would have died, too, had it not been for the sanatorium; and if one estimates conservatively the value of a human life, these 30 may have paid the expenses of that sanatorium for the year.

I have had largely to do with the Eudowood Sanatorium, and in the course of the years we have come gradually to the opinion which Dr. Wolman has expressed, that it is more economical to wholly cure a case than to half cure it. There is no economy in sending a patient away before he is ready and then having to take him back time after time. So that the policy of the Eudowood Sanatorium is to keep its patients until one thing or the other happens, either they are well, or they die.

At Eudowood we have arranged an "after cure," as it were, something which should be found in connection with all sanatoria, namely, a place where a patient, when he is seemingly well and yet not sufficiently well to withstand home conditions without danger of relapse, can stay for a time until fully recovered, and where he can work on the farm, care for chickens or rabbits until he is so thoroughly well that the danger of relapse after return to home and work is reduced to the minimum. We feel that this department has great economical value.

This question of length of stay has been raised at the State Sanatorium also. There the same conclusion is being arrived at, that in the future it is going to be wiser and more economical to keep patients for longer periods than in the past, so that the State Sanatorium, with its 400 beds, will probably follow the policy which Reisterstown and Eudowood have adopted.

What more can be done in Maryland? Although not apropos of the topics discussed, I want to say a word of the great problem we face in this state in regard to tuberculosis among the negroes. It is an ever-present topic and one full of seriousness, with 100,000 negro people in our midst especially susceptible to tuberculosis, mingling with the families of all our people, cooking, washing, serving and nursing the children. If any individual in the community is likely to be the carrier of infection, it is the negro. He is apt to be careless, ignorant and unappreciative, and so a menace not only to himself and his people, but also to the community in general. We are planning to attempt legislation in the coming winter to meet these conditions. Thus far there are no provisions in this state either for the incipient or the advanced case of tuberculosis among the negroes, except some 50 or 60 beds at Bay View, which are primarily reserved for pauper cases.

I wish to repeat what I said in the beginning: it would be very unfortunate for you to leave here to-night with the impression that the workers in the anti-tuberculosis crusade were discouraged, or were in any degree less enthusiastic in their work. While perhaps unduly hopeful of immediate results in the early days, they are still convinced that the disease can, under proper and sufficient methods and facilities, be continuously diminished in any community with much suffering saved and many lives restored to health and usefulness. Whether it can be wholly eradicated in the future is problematical, but, with the encouraging results already obtained before us, we cannot for one moment think of remitting our efforts to bring about this most desired end. Every one should put his shoulder to the wheel and give the best strength in him to this cause. You students who are going from here into many different communities in many parts of the country should aim to make yourselves strong, vital factors in this war against a disease which is destroying more men and women each year than all the fighting armies of Europe combined.

Dr. J. Hall Pleasants: The development of local institutional care of the tuberculous is interesting as we look back over the past 10 years. The movement really started at Eudowood several years before the Phipps opened, and for the first few years all classes of patients were taken there. As soon as the point of view which Dr. Hamman emphasizes was generally accepted Eudowood began to seek only early cases. Then followed soon afterwards the development of the State Sanatorium, at first largely devoted to the care of early cases. Later at both institutions emphasis was also laid upon the care of advanced cases, showing the tendency to look at the problem from the community standpoint rather than from the standpoint of the individual.

I think it might be interesting to some of you to know what

the institutional facilities are at present for the care of the tuberculous in Maryland. There are approximately 800 beds for Maryland, and of that number something over 500 are available for the tuberculous patients from Baltimore. The State Sanatorium can now handle 450 patients; about one-half of these coming from the counties, and the other half from the city. Eudowood has 100 beds and Bay View slightly under 200. There are accommodations at the Hebrew Hospital for about 55 patients. These are the four important institutions of the state. Over one-half of the beds for city patients are open to the poor of Baltimore, and are paid for, either in whole or in part, by the city. A good deal of money is expended and, of course, it is important to get the very best results. The funds available for the purpose are limited. The amount spent annually by the city and by the state is upwards of $200,000, and this sum does not include the cost of new construction. This is a large expenditure and, on the whole, is spent wisely. Perhaps it is just as fortunate that we have not tried to go ahead quite so rapidly as at one time we hoped to do before the situation was so thoroughly understood as it is now.

There are at present not sufficient accommodations for negroes and certain other classes of cases from Baltimore. On the other hand, to a certain extent, what can perhaps be spoke of as "the unstimulated demand" has already almost been met. If we want to encourage more patients to enter the hospitals we must give them better hospitals and better care than are offered by some of those now in existence. At Bay View, for instance, I doubt very much if we could get many more patients in a hospital of the character which we now have, even if we had more beds, as a certain stigma is still attached in the minds of the people to an institution very closely associated with an almshouse. On the other hand, if we had a municipal hospital of a distinctly better grade, offering better nursing care and greater physical comforts than can be obtained at some of the hospitals now receiving cases from Baltimore, we could get a larger number of patients to enter it. If all of the hospitals would readmit patients, I think the call for additional beds would be considerably increased. It is a difficult problem, and we seem to be going slowly; yet when we look back over the 10 years covered by Dr. Hamman and by Dr. Wolman we see that a good deal has actually been accomplished in providing hospital care.

DR. WOLMAN: I hate to take up any more time, but there is one statement I do not like to pass by, even from a friend, and that is that there are enough beds to meet the demand. This is true only with the vicious system we now have of not keeping patients long enough, which should be kept in mind. If the patients are kept long enough, we shall not have enough beds.

DR. JANEWAY: In summing up the results of the tuberculosis work here, I think we all feel that The Johns Hopkins Hospital owes a great deal to Dr. Hamman for the work that he has done in developing the Phipps Dispensary during these 10 years and for the kind of scientific publications that have appeared. The organization of the work and the men that he has brought together on the staff of that institution are things of which he should be very proud. In particular, I think we should recognize how important Dr. Hamman has made himself and how exceedingly valuable he has made his opinion in all tuberculosis matters, as the result of his 10 years' work in this branch of the hospital.

We now look forward to a new period and I hope you all feel that the Laennec Society is a place where you actively participate in the tuberculosis movement, which is now entering upon a somewhat new phase and in which the educated physician is to play an increasingly important rôle. It is therefore incumbent upon all of us to become educated physicians in respect to the attack on the problems of tuberculosis.

CONCERNING THE OCCURRENCE OF TUBERCLE BACILLI IN THE CIRCULATING BLOOD.

By C. R. AUSTRIAN and LOUIS HAMMAN.

I. INTRODUCTION.

Examination of the bodies of individuals dead of pulmonary tuberculosis or of other localized tuberculous disease almost constantly reveals tubercles scattered through organs and tissues other than those predominately affected. These tubercles are usually few in number and in an early stage of development. Their location justifies the assumption that as a terminal event in tuberculous disease tubercle bacilli invade the blood stream. Likewise, the obvious details of miliary tuberculosis can be explained only by accepting that under favorable mechanical conditions the blood is suddenly surcharged with tubercle bacilli. These well-established observations have been universally confirmed, but pathological anatomy offers no facts to prepare us for the astonishing results of more recent bacteriological investigations which would persuade us to believe that a bacillemia constantly accompanies tuberculous infections. Indeed, our credulity is taxed to this extreme, namely, we are told that tubercle bacilli occur in the blood not only of the manifestly tuberculous, but also of those with latent tuberculous foci, not singly, but in large numbers.

It is unnecessary to comment upon the violence these claims do our established notions about tuberculosis. They are revolutionary and demand a complete change of our fundamental views upon the nature of tuberculous infection and the course of tuberculous disease. Besides, they have received wide recognition and at present figure prominently in the arguments and generalizations that adorn tuberculosis literature. Therefore, it is important critically to review the data upon which these claims rest, and to furnish additional evidence that may aid to solve the difficulty.

We will review the situation briefly and in outline, since a number of excellent and detailed accounts of the numerous pertinent investigations have but recently appeared.[1] Shortly after the discovery of the tubercle bacillus many pathologists demonstrated acid-fast organisms in the blood of corpses dead of miliary tuberculosis, and a little later clinicians occasionally found them during life in the blood of patients suffering from the same disease. This discovery caused no surprise, for the facts only confirmed established views about the nature of miliary tuberculosis. Indeed, before the discovery of the tubercle bacillus, Villemin had successfully inoculated animals with the blood of tuberculous bodies, and Baumgarten had con-

[1] Elsässer; Rothacker and Charon; Berry; Haas; Klemperer; Hage; Klopstock and Seligmann.

firmed these results with the method of inoculating into the anterior chamber of the eye. However, it was generally conceded that, although tubercle bacilli invade the blood stream in miliary tuberculosis, still in local tuberculous infections no bacillemia occurs, and that even in advanced stages of pulmonary tuberculosis tubercle bacilli are carried by the blood only intermittently and in small numbers. The first communication to ruffle the settled calm of this conviction came from Liebmann in 1891, who claimed that the blood of patients treated with tuberculin contains numerous tubercle bacilli, whereas he was unable to demonstrate them in the blood of patients not so treated. Attempts to confirm these results failed, and Kossel ended the dispute when he was allowed to examine Liebman's slides, and pronounced his results to be due to faulty technic.

After this demonstration, interest in the occurrence of tubercle bacilli in the blood subsided, and during the following 15 years was only occasionally aroused. Thus Jousset, in 1904, by the method he names inoscopy, found tubercle bacilli in the blood of 11 out of 35 cases of pulmonary tuberculosis. Other French observers with the same and similar methods corroborated these results, but animal experiments, that is, injecting the blood into guinea pigs, gave a much lower percentage of positive findings. For instance, Bergeron found only 2 positive of 36 examined; Gary 5 out of 35. In Germany Lüdke's results attracted attention; by injecting intraperitoneally into guinea pigs from 5 to 10 cc. of blood withdrawn from the arm vein of tuberculous patients, 5 of 17 animals developed tuberculosis. Liebermeister, in 1909, reported examining the blood of 50 cases of pulmonary tuberculosis by inoculating guinea pigs intraperitoneally and thus demonstrating tubercle bacilli in 20. Although most of the patients had far-advanced pulmonary disease and many were examined shortly before death, still these results stand so prominently in contradiction to the experience of other investigators that they will receive further notice.

In this country interest was rudely awakened by the reports of Rosenberger. In 1909 this investigator published his results of the microscopical examination of the centrifugalized sediment of citrated blood from 49 cases of tuberculosis in all stages, claiming to have discovered tubercle bacilli in every instance. In a later report the number is increased to 300, all positive. This startling announcement led at once to control investigations here and in England, with the result that similar experiments undertaken upon tuberculous individuals and tuberculous cattle failed completely to verify Rosenberger's claims. The corroboration of Forsyth in England and Marshall and Petty and Rogers and Murphy in America furnishes isolated differences from the general testimony. The source of these conflicting results received a satisfactory explanation when Brem, followed by many other workers,[2] demonstrated the frequent contamination of distilled water with acid-fast bacilli. Since then opinion in this country has remained unshaken, and until recently no investigations of importance have been added to the subject.

[2] Holmes; Beitzke; Lehmann.

During the same period extensive researches were being pursued in Germany which led to widely varying results, and these researches continuing actively to the present time have given rise to a vigorous polemic. In 1908 Staübli introduced the acetic-acid method for examining the blood for organisms and during the following year Schnitter further improved the procedure by adding antiformin digestion. Subsequent investigations have been carried out almost entirely by the acetic-acid-antiformin method, a method, although tedious in detail, still simple in conception. The accompanying table shows at a glance what results have been obtained. The table is not constructed with any pretense to completeness, but with the desire to illustrate briefly and strikingly the divergence of the results. As may be seen, investigators differ to this extreme, whereas some find tubercle bacilli in the blood of all patients with tuberculous disease, be it early or advanced, others fail to find them even in the most advanced stages of the disease. Between these extremes there is every grade of difference. A few authors push the matter to the apparently ridiculous length of finding tubercle in the blood of individuals with latent tuberculous lesions and Kurashige to the inconceivable

Year.	Author.	Microscopically.		Animal inoculation.	
		Number of cases.	Per cent positive.	Number of cases.	Per cent positive.
1909	Schnitter	38	32	...	...
	Rosenberger	300	100	...	...
	Lippmann	25	44	...	...
	Liebermeister	...	...	50	40
1910	Jessen and Rabinowitsch	36	28	...	...
1911	Kurashige	155	100	...	...
	Sturm	50	22	50	46
	Krause	132	25	...	...
	Kennerknecht	68	100	13	100
	Susuki and Takaki	517	98	...	...
1912	Rumpf	43	67	35	8
	Hilgermann and Lössen	64	25	...	...
	Bacmeister and Rueben	?	100	15	0
	Nobecourt and Darre	...	...	40	10
	Liebermeister	100+	48	...	...
	Klemperer	14	86	...	...
	Bogasau	41	5	41	0
	Fraenkel	51	10	51	14
1913	Krabel	35	57	...	...
	de Verbizier	15	0	15	0
	Rogers and Murphy	50	100	...	...
	Bernard et al	36	11	...	...
	Rist et al	50	14	50	0
	Lange and Lindemann	78	0	...	...
	Rothacker and Charon	...	...	46	2
	Elsässer	41	7	15	0
	Querner	...	...	37	0
	Faginoli	81	100	...	...
	de Amicus	...	...	30	0
	Fraenkel	18	22	25	8
	Moewes and Bräutigam	30	0	50	0
	Rueben	24	100	13	0
	Kachel	26	35	26	15
	Brandes and Mau	40	45	...	...
	Mayer	25	20	25	0
1914	Baetge	38	0	46	37
	Fisher	13	0	13	0
	Haas	24	46	24	0
	Klopstack	49	18	49	0
	Lehmann	...	...	104	6
	Berry	51	0	...	...

point of claiming to diagnose a fresh tuberculous infection by the presence of bacillemia even before the development of tuberculin hypersensitiveness as manifested by cutaneous reactivity.

It is needless to review the many possible sources of error in examining blood preparations for tubercle bacilli. The matter has received repeated and extended consideration.[3] These possibilities are acknowledged by those who find tubercle bacilli most frequently, for they claim to have employed a scrupulous technic specifically to guard against this error. However, in view of the many negative results published by experienced and careful investigators, one is justified in assuming an attitude of skepticism towards positive microscopical findings, at least so far as to demand that the burden of proving the identity of the acid-fast organisms or particles found shall rest upon those who claim to discover tubercle bacilli so constantly in the blood.

The results of animal experiments cannot be so lightly disregarded. What this method of investigation has revealed is also shown in the table, and a glance discovers that the positive findings fall far below the proportions established by the microscopical method. However, the variation between the results of individual observers is hardly less astonishing. One author obtains constantly positive results, another in nearly half his cases; whereas many are able to demonstrate the presence of tubercle bacilli only occasionally even in advanced stages of tuberculous disease. The methods employed are reasonably uniform, consisting commonly in the intraperitoneal injection into guinea pigs of from 1 to 5 cc. of blood immediately upon withdrawal from the patient. Some have employed the sediment of from 1 to 10 cc. of blood treated by various methods of digestion, usually the acetic-acid-antiformin method; some, instead of inoculating intraperitoneally, have preferred subcutaneous injection into the groin. However, these procedures should in the main give generally comparable results and do not, taken alone, explain the existing discrepancy. Inoculation tuberculosis is a reasonably concrete and well-defined manifestation, for although certain confusing conditions do occur, still with care they may be differentiated from tuberculosis and they are not encountered frequently enough to be a satisfactory pretext for ignoring positive findings. When an author of experience states that so many inoculated animals developed tuberculosis, one cannot, in the absence of specific details, go behind the return and question the interpretation. The result must be credited, no matter how much at variance it stands with the experience of another, until more extended work decides the dispute. However, some authors do speak generally and some in detail about their animal results and upon these we may venture to comment.

A number of these authors disregard pathological-anatomical data and are content to diagnose inoculation tuberculosis in the absence of anatomical lesions when they find tubercle bacilli (we had better say acid-fast bacilli) in the sediment from the digested organs of the inoculated guinea pig.[4] Indeed, some animals are labeled tuberculous because in turn tubercle bacilli are found microscopically in their blood. Certain authors go still further and rest the diagnosis of inoculation tuberculosis upon finding Gram-positive rods and Much granules in smears from organs and in the sediment of organs digested with antiformin.[5] Excluding the results thus acknowledged to have been won by methods which are obviously unreliable, there stands out still in contrast with the results of many other observers the high positive proportion of Liebermeister. Liebermeister's report is a lengthy one, with full protocols, and the work therefore is open to inspection. For the details of a criticism of his experiments we refer you to the comments made by Kahn. Kahn points out that none of Liebermeister's results are controlled by histological examination; that in some instances the diagnosis of tuberculosis rests solely upon the discovery of acid-fast rods in smears of the organs, for instance, in one animal that died two days after inoculation; that his description of lesions lacks precision, for in some instances he calls the lesions tuberculous because smears show acid-fast rods, while in other instances the same lesions are pronounced not tuberculous because smears fail to reveal tubercle bacilli; that in some animals that died shortly after inoculation, in one instance on the sixth day, he describes caseous areas at the point of inoculation, a result hardly possible unless the animal had previously had tuberculosis. Kahn's points are well taken, and they encourage the conviction that Liebermeister has diagnosed too leniently.

It is apparent from the table that the microscopical method has far more positive results than the method of guinea pig inoculation. Fischer has collected from numerous reports 3495 cases examined microscopically with 44 per cent positive results, whereas, a similar collection of 1250 cases examined by animal inoculation yields but 17 per cent positive. Those authors who are convinced of the accuracy and reliability of microscopical examinations have sought to meet this difficulty with ingenious explanations. Their arguments may be briefly summarized as follows:

1. Only a small number of tubercle bacilli are present in the blood, and although these may be found microscopically, still they are not numerous enough to infect a guinea pig.

2. The tubercle bacilli present in the blood are weakened, that is, they have so far lost their viability that they can no longer infect.

3. When the blood of tuberculous individuals is injected into guinea pigs, not only tubercle bacilli but immune bodies as well are introduced. The immune bodies inhibit the growth of the tubercle bacilli and prevent infection.

We have neither the space nor the inclination to enter this field of abstract speculation. It would be difficult to prove or disprove arguments 2 and 3, but what evidence we possess does not strongly favor them. As regards the first argument, our own experience (and the experience of many others) leads us to believe that the guinea pig is a more delicate indicator of the presence of tubercle bacilli than the microscopical examination of the sediment of much manipulated blood. But

[3] Hage; Fischer; Kahn; Gobel; de Amicus; Bogasau; Rumpf; Frankel.

[4] Kennerknecht.

[5] Sturm.

anyone interested may read the arguments for, in Klemperer and Liebermeister; against, in Kahn and Fischer.

As one would presume, the conflicting evidence concerning the occurrence of tubercle bacilli in the blood of human beings has led many investigators to seek more reliable data from animal experiments. However, in this direction one is immediately met by the difficulty of reproducing analogous conditions. Leaving aside the miliary form, tuberculosis in human beings is relatively a local disease during the greater part of its course. In animals it is difficult to regulate the conditions of infection so as to imitate this important feature of the disease in man. Following intravenous inoculation, the usual procedure for rabbits and guinea pigs, the tuberculous lesions predominate in the lungs, but the disease is seldom restricted and even early in its course other organs, notably the spleen and liver and kidneys, are extensively involved. Thus conditions more nearly parallel general tuberculosis than the local types usually found in man. The result does depend somewhat upon the infecting dose, for the same culture administered in large quantity may produce a rapidly fatal general infection, whereas, when a small amount is given, only scattered foci appear in the lungs and the animal may live for months. Under the former conditions one would expect to find tubercle bacilli in the blood constantly, whereas under the latter they might appear infrequently and demonstrably only towards the end of the disease. Results that we shall give later confirm this supposition. The virulence of the organism is likewise of importance. As Hess has shown in his interesting experiments, virulent types remain longer in the blood and reappear earlier than less virulent types. One is prepared, therefore, to find great divergence amongst the results obtained upon animals, and the expectation is fully confirmed by published reports. Tuberculous disease in cattle is somewhat nearer the human type than experimental infections in rabbits and guinea pigs, and examination of the blood of tuberculous cattle has yielded almost uniformly negative results.[6]

Although many isolated investigations upon the infectiousness of the blood of tuberculous animals had previously been made, the first extensive report upon the subject appeared in 1907 from Marmorek. He found that after subcutaneous inoculation of guinea pigs tubercle bacilli appear in the blood from 30 to 60 days later; after inoculation into the anterior chamber of the eye somewhat earlier; and still earlier after intraperitoneal inoculation. Injected into the arterial blood stream tubercle bacilli disappear from the blood in from 1 to 2 days to recur 5 to 14 days later; injected intravenously they disappear in from 1 to 2 hours to recur from 2 to 6 weeks later. Hess confirms these results in part, since he finds that virulent organisms remain in the blood from a few to 27 hours after intravenous injection and that they then disappear to return again 4 to 5 weeks later when the animal has become extensively tuberculous. The occurrence of tubercle bacilli in the blood has been investigated upon animals just as upon human beings, both microscopically and by guinea pig inoculation. Concerning the microscopical method, it need only be said that the same confusing results are obtained as were commented upon in considering the results of the method applied to human beings, namely, some claim to find them constantly, others in a large proportion of the animals, still others in healthy as well as in infected animals. The results obtained by guinea-pig inoculation are almost as confusing. No doubt the severity of the infection, the virulence of the infecting organism and the interval after infection that the examination is made explain much of the discordance.

Finally, we would point to the further confusion that Rabinowitsch has precipitated by renewing the claim that tuberculin mobilizes tubercle bacilli. Although unable to demonstrate tubercle bacilli in the blood of tuberculous animals before tuberculin is given, she finds them frequently after the injections. Bacmeister confirms these results upon human beings. Of 15 individuals whose blood was negative by animal inoculation, 4 became positive after a diagnostic tuberculin reaction. Mayer, Moewes, Liebermeister, Storath, Lange and Lindemann fail to confirm Bacmeister's results. Hage and Fischer have published extensive experiments upon animals and disagree with Rabinowitsch's conclusions.

II. AUTHORS' RESULTS.

During the past two years the authors have been interested in the question of the occurrence of tubercle bacilli in the circulating blood, and since each has worked quite independently of the other, the results, which in the main agree, are therefore more strikingly confirmed. It is thought best to present the contributions separately and at the end to summarize the results and draw the conclusions that the work fully warrants:

A. Investigations of Dr. Charles R. Austrian.

The work herewith briefly reported has been carried on through a period of some 20 months. It will be dealt with under two main captions:

1. Clinical—Experimental.
2. Experimental.

1. *Clinical—Experimental.*—The blood of 50 individuals with pulmonary tuberculosis was studied. Twenty of the patients were in Stage I of the disease; 15 were in Stage II, and 15 in Stage III. All of them showed, in addition to definite physical signs of pulmonary infection, tubercle bacilli in the sputum, or a positive tuberculin reaction and in many both examinations gave positive results.

Specimens of blood obtained by puncture from a vein in the antecubital fossa, or forearm, were studied according to the following methods:

(a) Stained Preparations:

Five cubic centimeters of blood aspirated in a sterile syringe (Record) from a vein of the forearm were placed in a sterile flask containing 10 cc. of 3 per cent acetic acid and shaken thoroughly, avoiding the formation of foam. The mixture was allowed to stand for 30 minutes and was then decanted into

[6] Schroeder and Cotton; Sawyer; Broll; Mohler; Titze, Thieringer and John.

2 sterile centrifuge tubes and centrifugalized for 45 minutes at the rate of about 2500 revolutions per minute. The supernatant red fluid was then removed; to the sediment 5 volumes of 33 per cent antiformin were added and after standing for from 1 to 6 hours the preparation was shaken until clear. Doubly distilled water was now added and the suspension was rotated for one hour at 2500 revolutions per minute. The white sediment, washed 3 times with doubly distilled water, was then spread on two new glass slides that had been thoroughly cleaned with alcohol and sterilized by dry heat. The spreads were fixed by heat in a sterile Petri dish, dried in the thermostat and stained by the Ziehl-Nielson method.

It is important to emphasize that extreme care was taken in cleaning all glassware employed. Flasks were boiled with alkali, washed with distilled water, alcohol and ether and sterilized by dry heat.

For the sake of brevity, suffice it to say that careful examination of such preparations made from the blood of 25 patients with manifest pulmonary tuberculosis in no instance revealed the presence of the tubercle bacillus. This in spite of the fact that the slides were each examined for from one to two hours, the fields slowly searched with the aid of a mechanical stage.

In only a few instances were a few acid-fast granules found and these could not have confused an observer familiar with the morphology or the staining properties of the bacillus tuberculosis.

These negative findings so at variance with the results of numerous observers led to the use of the method of inoculation with the idea that it might prove more delicate.

Technic.—(a) From a vein of the forearm 10 or 15 cc. of blood were aspirated into a clean sterile Record syringe and immediately mixed with 1.5 to 3 cc. of sterile 1.5 per cent sodium citrate solution to prevent coagulation.

From 4 to 7.5 cc. of the citrated whole blood were injected into the peritoneal cavity of a guinea pig. After six or eight weeks the animal was etherized and examined for evidences of tuberculous infection.

This procedure was carried out in 25 cases with completely negative results.

(b) Ten or 15 cc. of blood obtained according to the method described above were defibrinated by shaking with sterile glass beads. Inoculation experiments made with blood so prepared were carried out with specimens obtained from 15 cases of pulmonary tuberculosis. In not one of the inoculated guinea pigs was any sign of tuberculous infection found.

(c) The intraperitoneal injection into guinea pigs of varying quantities of serum, obtained from tuberculous individuals likewise failed to cause infection.

(d) The intraperitoneal injections of the antiformin insoluble residue of 10 or 15 cc. of blood from infected patients did not lead to the development of tuberculosis in the animals.

Pulmonary tuberculosis in man is generally a localized infection and to obtain from an examination of the blood of animals data comparable to the facts furnished by the study of human blood, the attempt was made to produce a similar localized pulmonary infection in animals. This was readily accomplished by the use of Meltzer's method of intratracheal injection.

II. *Experimental Part.*—Rabbits weighing from 1700 to 2800 gm. were chosen.

The rabbit was etherized and placed on its back in such a position as to permit extension of the neck over the end of the operating board. The mask was then removed, a gag placed in the mouth and slowly, gently, a fine rubber catheter was passed through the mouth into the trachea. To facilitate the passage of the tube a close-fitting copper wire tipped with a blunt lead was kept in the catheter and this was not withdrawn until a proper insertion had been obtained. Evidence of the entrance into the trachea was furnished by reflex cough and apnea; and by the grating of the lead tip along the tracheal rings, the hand recognized the passage of the sound within the trachea.

When the catheter was in place the wire was withdrawn and a sterile syringe partly filled with material for injection fixed to it. Transmission of a wave through this fluid with each respiratory phase, again confirmed the position of the tube. Under slight pressure the material for injection was now slowly introduced.

In the following experiments suspensions of tubercle bacilli A1 and H39 in 0.85 per cent salt solution were employed:

A1. *A Bacillus Tuberculosis of Avian Type.*—This organism was obtained four years ago from an outside source and was fully identified as of the avian variety. It grew rapidly and luxuriantly on glycerine agar and was of only slight virulence.

H39. *A Bacillus Tuberculosis of Human Type.*—The culture was obtained from the Saranac Laboratory through the kindness of Dr. Allen Krause—a typical bacillus tuberculosis, typus humanus, and of constant virulence.

The suspensions of these bacilli used in the experiments recorded below were prepared as follows:

The growth on a slant of glycerine agar was placed in a sterile flask that contained sterile glass beads, thoroughly shaken with 0.85 per cent salt solution until a fairly homogeneous suspension was obtained and this was filtered through sterile cotton to remove coarse clumps. This suspension was then diluted with 0.85 per cent salt solution until it was of the turbidity of a 36-hour broth culture of Bacillus typhosus. From 2 to 3 cc. of this material were injected into the trachea.

Thirty-six rabbits received intratracheal injections of one or the other strain. Six died from trauma received as a result of faulty technic in passing the catheter, 5 succumbed to intercurrent infection and showed no gross evidence of tuberculosis, and 25 developed pulmonary tuberculosis. In only 10 of the latter did a disseminated infection develop.

At varying intervals of from 2 to 5 days the blood of these animals was examined for the presence of tubercle bacilli. The methods employed were those above described in connection with the study of human blood—examinations of stained smears, inoculations into guinea pigs of citrated whole blood, of blood defibrinated by whipping and of serum. The quantities of blood used in these tests varied from 5 cc. aspirated from the heart by punctures to the entire blood content of the rabbit.

In four instances all of an animal's blood was utilized in making smear preparations on two slides. In four other experiments the blood of one rabbit was injected into the peritoneal cavities of two guinea pigs. In every case a complete autopsy was made of the donor of blood for smear preparations or for reinoculation experiments, and the anatomical findings are here briefly presented.

The following types of lesions were found:

(a) A gelatinous lobar pneumonia in gross resembling the variety occasionally seen in man.

(b) A diffuse caseating broncho-pneumonia at times causing a pseudolobar consolidation.

(c) A combination of these two varieties.

(d) Extensive cavity formation in the lungs.

Although bacilli of low virulence were given in small numbers to resistant animals, a typical fibroid phthisis was never produced.

Following inoculation the rabbits generally showed no symptoms for 10 days. Then cough developed, at first paroxysmal, later becoming more constant. Within a few days emaciation became evident and rapidly progressed until death occurred.

At autopsy 12 to 39 days after infection no constant localization of the lesions in any one of the lobes of the lungs was noted, though the maximum involvement was usually found in either or both lower lobes.

In general the affected lung was more voluminous than the normal, often encroaching upon the opposite side of the thorax. Outspoken pleural exudate was not seen in any of the animals, but a thickened pleura or irregular nodulation, due to subserous tubercles, was frequently found.

The lungs in several of the animals showed a typical gelatinous pneumonia. The diseased lobe or lobes voluminous, firm, non air-containing; on section, moist, translucent, gray, mottled in the earlier cases (before 12 days) with hemorrhagic dots, in the later ones (after 18 days) dotted with small yellow caseating areas. The bronchi were usually filled with a grumous yellow exudate. With such a condition in one lobe of a lung an entirely differently appearing lesion was found in other portions of the same lung or in the opposite one. Either emphysema with areas of grayish red (early) or of caseating (late) broncho-pneumonia, or congested parenchyma with scattered miliary and confluent tubercles, was frequently present.

Instances of bilateral lobar or pseudolobar tuberculous broncho-pneumonia were frequent.

Cavity formation was found in 10 animals, the vomicæ varying in size from several millimeters up to that of an entire lobe. Generally they were multiple, honeycombing the entire pulmonary tissue. The walls were ragged and irregular, the contents typical caseous material. No eroded or isolated blood vessels were found, nor could secondary infection be demonstrated, even when communication of a cavity with a bronchus was apparent.

Microscopic examination of the lesions showed the following:

The alveoli were densely packed with leucocytes, the predominant type varying in different areas. In some there were many polymorphonuclears and relatively few mononuclears; in others the converse was true. Again, many contained numerous mononuclear leucocytes, large mononuclear endothelial cells and multinucleated giant cells. Many alveoli were loosely filled with a granular detritus, mononuclear leucocytes and red corpuscles.

The alveolar walls in many places were denuded of endothelium and the interalveolar vessels were congested.

In areas, the architecture of the lungs was completely destroyed, replaced by caseous material; or mere tags of alveolar walls remained. Necrosis apparently began in the exudate and spread from there, involving the lung parenchyma and the bronchi.

Typical tubercles fresh and in various stages of degeneration were numerous.

In places beginning repair was seen.

The bronchi in many places were dilated, their lumens containing an exudate rich in polymorphonuclear and mononuclear leucocytes, their walls in places ulcerated, the ulceration appearing to have spread from the alveoli.

The pleura showed thickening and infiltration with mononuclear leucocytes.

Tubercle bacilli were fairly numerous throughout the lesions.

In the 10 instances in which disseminated tuberculosis developed a few small tubercles were found in the kidneys and spleen.

It is interesting that in the series of experiments no one type of lesion was found at a constant time after infection, a variety that occurred early in one animal developing late in another, and vice versa.

The findings here recorded agree closely with those described by Lewis and Montgomery in their experiments dealing with bronchogenic infection of dogs with the tubercle bacillus, except that they did not find the development of a gelatinous pneumonia.

The results of the examination of the blood of the rabbits with localized pulmonary tuberculosis completely confirmed the findings obtained from the study of human blood already recorded. In none of the 15 rabbits in which the infection remained a local one were bacilli demonstrated in the circulating blood by the use of any of the methods described.

In 3 of the 10 animals that developed a systemic infection, tubercle bacilli were found in the blood. In one both stained smears and inoculation experiments gave positive findings; in one organisms were found in stained preparations, whereas a guinea pig injected intraperitoneally with blood remained free of tuberculosis; and in the third case the inoculation test was positive, though examination of stained smears failed to show the presence of any organisms.

B. Investigations of Dr. Louis Hamman.

1. *Clinical-Experimental.*—The blood of 24 patients with advanced pulmonary tuberculosis was examined for the presence of tubercle bacilli. The blood of two patients was examined twice, of another three times, a total of 28 examinations.

The patients all had far-advanced pulmonary tuberculosis; none had a lesion less extensive than Turban III, and all had well-marked local and general symptoms. Many of the patients were bedridden with high fever and night sweats at the time the examination was made. In all the diagnosis was confirmed by repeatedly finding tubercle bacilli in the sputum.

(a) *Microscopical Examinations.*—From 2.5 to 5 cc. of blood withdrawn from the arm vein were prepared by the Staübli-Schnitter method which has been outlined by Dr. Austrian. During the earliest investigations an elaborate process was followed in cleaning the glassware, subsequently only scrupulous cleanliness and hot air sterilization were used. Throughout the investigation only freshly distilled water was employed. The slides were examined on a mechanical stage and from one to two hours devoted to each specimen.

In not one instance was a single tubercle bacillus found. I make this statement positively, for in the examination of the slides I encountered no structures that left me hesitating about their identity; I mean about their being or not being tubercle bacilli. It is true that the first slides were the source of some little trepidation, since a few blue rods were seen which aroused fear, lest the method of treating the blood might destroy the characteristic staining reaction of the tubercle bacillus. This fear was promptly allayed when I found that tubercle bacilli added in small numbers to freshly drawn blood were recovered with unaltered staining properties after the blood had been passed through the usual routine.

(b) *Animal Inoculation.*—From 2.5 to 5 cc. of the blood of 20 of the patients above referred to were injected intraperitoneally into a guinea pig. Eight of the 20 animals died within 3 weeks after the injection, 6 of them, indeed, within 24 hours. Twelve animals lived for one month or longer. At autopsy none showed any lesion that could have been suspected of being tuberculous.

2. *Experimental.*—(A) Four rabbits were inoculated intravenously with a suspension of human tubercle bacilli in 0.85 per cent saline solution. The culture used was H39 previously described by Dr. Austrian.

Five cubic centimeters of blood were withdrawn from the heart in one instance after 5 hours; in another after 24 hours; in two instances after 19 days; in two instances after 44 days; in another instance after 45 days.

All four rabbits at autopsy showed extensive pulmonary tuberculosis and a few scattered tubercles in the spleen, liver and kidneys except one of the animals which died on the 24th day after inoculation and showed only pulmonary lesions.

In 5 of the 7 examinations the 5 cc. of blood were divided into two portions; 2.5 cc. were injected intraperitoneally into a guinea pig; 2.5 cc. were prepared by the Staübli-Schnitter method for microscopical examination.

In 2 of the 7 examinations the whole 5 cc. of blood were prepared for microscopical examination. Of the 7 microscopical examinations 2 were positive. In each instance 2 tubercle bacilli were found after prolonged search. One of the positive examinations was made 44 days after inoculation, the other 5 hours after.

Of the 5 guinea pigs inoculated intraperitoneally none showed any evidence of tuberculous infection; 1 animal died 4 weeks after inoculation, 2 after 6 weeks, 1 after 14 weeks, and 1 was sacrificed after 3 months. The 2 specimens of blood positive microscopically were both negative by guinea pig inoculation.

(B) Three rabbits were inoculated intravenously with a suspension of human tubercle bacilli (H39).

Twenty-two days after inoculation 5 cc. of blood were withdrawn from the heart; 2.5 cc. were prepared for microscopical examination; 2.5 cc. were injected intraperitoneally into a guinea pig.

Subsequently the rabbits received increasing doses of tuberculin and the blood was examined at intervals for tubercle bacilli. From 5 to 15 cc. of blood were withdrawn from the heart; from 2 to 5 cc. were injected intraperitoneally into a guinea pig; from 2 to 10 cc. were prepared for microscopical examination.

Rabbit No. 5 was sacrificed 78 days after inoculation. Autopsy showed diffuse caseous and fibroid tubercles scattered throughout the lungs; no tubercles in other organs.

Rabbit No. 7 was sacrificed 77 days after inoculation. Autopsy showed about 10 firm caseous nodules about 2 mm. in diameter scattered through the lungs; several small tubercles in the liver and spleen.

The protocol of experiment No. 6 is given in detail as an illustration:

RABBIT NO. 6.

February 5, 1914. Intravenous injection of suspension of human tubercle bacilli (Culture H39).

March 7. Five cc. blood withdrawn from the heart. Two and one-half cc. prepared by the acetic acid-antiformin method for microscopical examination. No tubercle bacilli found.

Two and one-half cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 24. No evidence of tuberculosis.

March 18. Subcutaneous injection of 0.025 cc. bouillon filtrate.

March 19. Five cc. blood withdrawn from the heart; 2 cc. prepared for microscopical examination. No tubercle bacilli found.

Three cc. injected intraperitoneally into guinea pig. Guinea pig died March 28, 1914. No tuberculosis found.

March 24. Subcutaneous injection of 0.1 cc. O. T.

March 30. Subcutaneous injection of 0.2 cc. O. T.

April 1. Subcutaneous injection of 0.25 cc. O. T.

April 2. Eleven cc. blood withdrawn from the heart; 6 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 24. No tuberculosis found.

April 7. Intravenous injection of 0.5 cc. O. T.

April 8. Twelve cc. blood withdrawn from the heart; 7 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig died April 17, 1914. No tuberculosis.

April 20. Intravenous injection of 1 cc. O. T.

April 21. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 27, 1914. No tuberculosis found.

April 27. Intravenous injection of 1 cc. O. T.

April 28. Fifteen cc. blood withdrawn from heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 27, 1914. A few small tuberculous nodules in the omentum and spleen. Verified microscopically.

April 29. Intravenous injection of 1 cc. O. T.

April 30. Fifteen cc. blood withdrawn from heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 27. Tuberculous nodules on peritoneal surface, in liver and in spleen. Tuberculosis in substernal lymph glands. Verified microscopically.

June 1. Rabbit extremely emaciated and moribund. Sacrificed. Extreme tuberculosis of the lungs, few scattered tubercles in the liver. Spleen normal. Microscopical sections showed extensive tuberculosis of the lungs. No tuberculosis in the spleen.

Rabbit No. 5 had six examinations of the blood. One was positive microscopically, one was positive by animal inoculation. The positive microscopical finding was on the 42d day after inoculation; the positive animal result on the 58th day.

The blood positive microscopically had no animal control; the blood positive by animal inoculation was negative microscopically.

Rabbit No. 7 had five examinations of the blood. All were negative, both microscopically and by animal inoculation.

Therefore, of 18 examinations of the blood of rabbits made from the 40th to the 86th day after inoculation with human tubercle bacilli, one was positive microscopically; three were positive by animal inoculation.

(C) Three rabbits were inoculated intravenously with a suspension of bovine tubercle bacilli (Culture B_1) in 0.85 per cent salt solution. A liberal dose was given with the intention of producing a rapidly fatal infection.

Culture B_1 is a typical culture of the bovine type of tubercle bacillus of low virulence obtained from the Saranac Laboratory through the kindness of Dr. Allen Krause.

Rabbit No. 8 died on the 29th day after inoculation, immediately after bleeding. Autopsy showed extensive tuberculosis of the lungs and spleen, and numerous tubercles in the liver and kidneys. A rent in the right ventricle was the cause of death. On the 28th day after inoculation 5 cc. of blood were withdrawn from the heart. Two cc. were prepared for microscopical examination. No tubercle bacilli found. Three cc. were injected intraperitoneally into a guinea pig; the guinea pig sacrificed three months later showed extensive tuberculosis of the spleen and liver. On the same day the rabbit received subcutaneously 0.05 cc. O. T.

On the 29th day after inoculation 5 cc. of blood were withdrawn from the heart. Ten cc. were prepared for microscopical examination. No tubercle bacilli found. Five cc. were injected intraperitoneally into a guinea pig; the guinea pig died five weeks later and no evidence of tuberculosis was found.

Rabbit No. 9 died 31 days after inoculation. Autopsy showed extensive tuberculosis of the lungs and spleen and numerous tubercles in the liver and kidneys.

On the 28th day after inoculation 5 cc. of blood were withdrawn from the heart. Two cc. were prepared for microscopical examination; no tubercle bacilli found. Three cc. were injected intraperitoneally into a guinea pig; guinea pig died 49 days after inoculation and showed extensive tuberculosis of peritoneum, spleen, liver, substernal glands and lungs.

On the same day rabbit received 0.05 cc. O. T. subcutaneously.

On the 29th day after inoculation 15 cc. of blood were withdrawn from the heart. Ten cc. prepared for microscopical examination; one definite tubercle bacillus found. Five cc. injected intraperitoneally into a guinea pig; guinea pig sacrificed three months later showed extensive tuberculosis of spleen, tubercles in the liver and a few small areas of tuberculous infiltration in the lung.

Rabbit No. 10 died on the 37th day after inoculation. Autopsy showed extensive tuberculosis of the lungs and a small number of tubercles in the liver, spleen and kidneys.

Blood withdrawn on the 28th, 29th and 37th days after inoculation was negative upon microscopical examination; a guinea pig inoculated upon the 28th day died 18 days later and showed no evidence of tuberculosis; guinea pigs inoculated on the 29th and 37th days developed extensive tuberculosis of the spleen and liver.

Therefore, of 7 examinations of the blood of rabbits four weeks after intravenous inoculation with a large dose of bovine tubercle bacilli, one was positive microscopically, five were positive by animal inoculation.

(D) Three rabbits were inoculated intravenously with a barely opalescent suspension of bovine tubercle bacilli (Culture B_1) in 0.8 per cent salt solution.

Rabbit No. 11, sacrificed 28 days after inoculation, showed at autopsy a number of firm tuberculous nodules scattered through the lungs and a few tubercles in the liver and spleen.

Rabbit No. 12, sacrificed 78 days after inoculation, showed numerous large caseous tubercles scattered through the lungs and a large spleen studded with tubercles.

Rabbit No. 13, sacrificed 28 days after inoculation, showed firm tuberculous nodules scattered through the lungs, but no tubercles in the other organs.

Upon these three rabbits 13 examinations of the blood were made during the period from the 14th to the 28th day after inoculation. During this period large doses of tuberculin were given intravenously. In each instance 15 cc. of blood were withdrawn from the heart; 5 cc. were injected intraperitoneally into a guinea pig; 10 cc. were prepared for microscopical examination. In no instance were tubercle bacilli demonstrated either microscopically or by animal inoculation. The protocol of experiment No. 11 is added.

RABBIT No. 11.

April 7, 1914. Intravenous injection of a suspension of bovine tubercle bacilli (Culture B_1).

April 21. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared by the acetic-acid-antiformin method for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 24, 1914. No evidence of tuberculosis.

Intravenous injection of 0.025 cc. O. T.

April 22. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig died May 27, 1914. No evidence of tuberculosis.

April 27. Intravenous injection of 0.1 cc. O. T.

April 28. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 27, 1914. No evidence of tuberculosis.

April 29. Intravenous injection of 0.2 cc. O. T.

April 30. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig died June 16, 1914. No evidence of tuberculosis.

May 4. Intravenous injection of 0.5 cc. O. T.

May 5. Fifteen cc. blood withdrawn from the heart; 10 cc. prepared for microscopical examination. No tubercle bacilli found.

Five cc. injected intraperitoneally into guinea pig. Guinea pig sacrificed June 27, 1914. No evidence of tuberculosis.

May 5. Rabbit sacrificed. Autopsy shows a few small firm nodules scattered throughout the lungs, and a few tubercles in the liver and spleen. Confirmed microscopically.

SUMMARY.

In pulmonary tuberculosis the authors were unable to demonstrate the presence of tubercle bacilli in the blood in a single instance notwithstanding the fact that many of the patients when examined were in the last stages of the disease.

In animals, when the disease remains localized in the lungs, tubercle bacilli are not found in the circulating blood. When the disease becomes generalized, as it does in the late stages of pulmonary infection and very soon after overwhelming intravenous injections, circulating tubercle bacilli are frequently demonstrable.

The evidence presented points strongly against the mobilization of tubercle bacilli by the injection of tuberculin.

A larger number of positive results was revealed by the method of animal inoculation than by the microscopical examination of the sediment obtained by treating blood according to the acetic-acid-antiformin method.

BIBLIOGRAPHY.

de Amicus: Int. Centralbl. f. d. gesamte Tuberkuloseliteratur, 1913, VII, 645.

Bacmeister and Rueben: Deut. med. Wchnschr., 1912, XXXVIII, 1535.

Baetge: *Ibid.*, 1914, XL, 591.

Beitzke: Berl. klin. Wchnschr., 1910, XLVII, 1451.

Bergeron: Thèse de Paris, 1904.

Bernard: Ann. de méd., Paris, 1914, I, 217.

Bernard, Debri and Baron: Bull. Soc. d'étude scient. sur la tuberc., 1913, III, 52.

Berry: Jour. Infect. Diseases, 1914, XIV, 162.

Bogason: Int. Centralbl. f. d. gesamte Tuberkuloseliteratur, 1913, VII, 644.

Brandes and Mau: Deut. med. Wchnschr., 1913, XXXIX, 1137.

Brem: Jour. Am. Med. Asso., 1909, LIII, 909.

Broll: Berl. Tierärtz. Wchnschr., 1909.

Burvill-Holmes: Am. Jour. Med. Sc., 1910, CXXXIX, 99.

Elsässer: Beitr. z. Klin. d. Tuberk., 1913, XXVI, 367.

Faginoli: Int. Centralbl. f. d. gesamte Tuberkuloseliteratur, 1913, VII, 647.

Fisher: Ztschr. f. Hyg. u. Infektionskrankh., 1914, LXXVIII, 253.

Forsyth: British Med. Jour., 1909, I, 1001.

Fränkel, F.: Deut. med. Wchnschr., 1913, XXXIX, 737.

Fränkel, C.: Int. Centralbl. f. d. gesamte Tuberkuloseliteratur, 1913, VII, 316.

Gary: Thèse de Lyon, 1904.

Göbel: Deut. med. Wchnschr., 1913, XXIX, 1136.

Haas: Beitr. z. klin. Chir., 1914, XC, 78.

Hage: Beitr. z. Klin. der Tuberk., 1914, XXXI, 71.

Hess: Arch. Int. Med., 1912, X, 577.

Hilgerman and Lössen: Deut. med. Wchnschr., 1912, XXXVIII, 895.

Jessen and Rabinowitsch: Deut. med. Wchnschr., 1910, XXXVI, 1116.

Jousset: Sem. méd., 1904, XXIV, 289.

Kachel: Beitr. z. Klin. d. Tuberk., 1913, XXVIII, 275.

Kahn: Münch. med. Wchnschr., 1913, X, 345.

Kennerknecht: Beitr. z. Klin. d. Tuberk., 1912, XXIII, 265.

Klemperer: Therapie der Gegenwart, 1912, LIII, 433; Berl. klin. Wchnschr., 1914, LI, 436.

Klopstock and Seligman: Ztschr. f. Hyg. u. Infektionskrankh., 1914, LXXVI, 77.

Kossel: Berl. Klin. Wchnschr., 1891, XVIII, 470.

Krabbel: Deut. Ztschr. f. Chirugie, 1913, CXX, 370.

Krause: Ztschr. f. Tuberk., 1911, XVII, 436.

Kurashige: *Ibid.*, 347.

Lange and Lindemann: Centralbl. f. Bakteriologie, 1913, LVII, 285.

Lehmann: Deut. med. Wchnschr., 1913, XXXIX, 1556.

Lehmann: Beitr. z. Klin. d. Tuberk., 1914, XXX, 477.

Liebmann: Berl. klin. Wchnschr., 1891, XVII, 97, 303.

Liebermeister: Med. Klin., 1912, VIII, 1018; Virchows Arch., 1909, CXCVII, 332.

Lippmann: Münch. med. Wchnschr., 1909, LVI, 2214.

Lüdke: Wien. klin. Wchnschr., 1906, XIX, 949.

Marmorek: Berl. klin. Wchnschr., 1907, XLIV, 18.

Mayer: Ztschr. f. Tuberk., 1913, XXI, 447.

Mendenhall and Petty: Jour. Am. Med. Ass., 1909, LIII, 867.

Moewes and Bräutigam: Deut. med. Wchnschr., 1913, XXXIX, 231.

Moewes: Deut. med. Wchnschr., 1914, XL, 491.

Mohler: Bull. No. 116, U. S. Dept. of Agriculture.

Nobecourt and Darre: Bull. Soc. d'étude scient. sur la tuberc., 1912, II, 176.

Querner: Münch. med. Wchnschr., 1913, LX, 401.

Rabinowitsch: Berl. klin. Wchnschr., 1913, L, 110.

Rist, Armand-Delille and Levy-Bruhl: Bull. Soc. d'étude scient. sur la tuberc., 1913, III, 9.

Rogers and Murphy: Jour. Am. Med. Ass., 1913, LX, 995.

Rosenberger: Am. Jour. Med. Sc., 1909, CXXXVII, 267.

Rothacker and Charon: Centralbl. f. Bakteriologie, 1913, I, Abt. Bd. LXIX, 478.

Rueber: Freiberg, 1913.

Rumpf: Münch. med. Wchnschr., 1912, LIX, 1951.

Sawyer: Arch. Int. Med., 1909, IV, 637.

Schnitter: Deut. med. Wchnschr., 1909, XXXV, 1566.

Schroeder and Cotton: Arch. Int. Med., 1909, IV, 133.

Staubli: Münch. med. Wchnschr., 1908, LV, 2601.

Storath: Ztschr. f. Tuberk., 1914, XXII, I.

Sturm: Beitr. z. Klin. d. Tuberk., 1911, XXI, 239.

Susuki and Takaki: Centralbl. f. Bakteriologie, 1911, LXI, 149.

Titze, Thieringer and John: Arbt. aus. d. Kaiserl. Gesundheitsamt, 1913, XLIII.

de Verbizier: Rev. de méd., 1913, XXXIII, 161.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

MAY 3, 1915.

1. The Use of a Celluloid Tube in Adding Length to the Terminal Phalanx of a Finger, After Traumatic Loss of Tissue. DR. J. S. DAVIS.

When a partial traumatic amputation of the terminal phalanx of a finger takes place, one of two conditions is found: Either the part is cut away clean with little damage to the remaining portion, or the part is crushed off, and the tissues adjacent to the amputated portion are more or less traumatized. After the ordinary healing by granulation we often find a sensitive stump in which the bone is covered only by a thin scar.

The question arises as to the best method of early treatment, especially when the bone is exposed.

In order to obtain a good functional result we must contrive to place a pad of tissue over the bone. This may be done rapidly and satisfactorily by shortening still more the exposed bone and closing the soft parts over it, but this method gives a shorter stump.

In certain occupations the loss of all or a portion of the terminal phalanx of a finger is a matter of considerable economic importance to the skilled worker. It is often advisable to preserve the remaining length of the finger, and if possible to replace the loss of tissue, thus giving a more useful and less painful stump, and at the same time one which is less disfiguring.

After seeing a number of these cases, it occurred to me that some procedure might be devised by which this object could be accomplished. One should always replace the amputated portion unless it is too much traumatized, or unless a period longer than 3 or 4 hours has elapsed between the time of the accident and the first treatment. This procedure is attended with little danger and if the replaced portion does not regain its vitality it can be easily removed, and the building up process then inaugurated.

The advisability of tissue transplantation suggested itself at once, and the method of utilization of pedunculated flaps from the chest or abdominal walls to replace the loss was considered. However, this method can only be carried out in the hospital, as constant supervision of the patient is essential on account of the irksome position necessary.

The majority of the patients with these injuries are treated in the Out-Patient Department, so a method must be used which will give good results without the necessity of admission to the hospital.

The most promising procedure seemed to be that of stimulating the growth of granulation tissue on the end of the stump, and in some way to confine the growth to the desired size and direction.

In searching for means to accomplish this I thought that a stiff non-adhesive material which could be wrapped around the finger, would be satisfactory. After a number of experiments I found that sheet celluloid 1/200 of an inch thick would be best for the purpose. This material was transparent and could be cut in a pattern, which, when rolled, formed a tube adjustable to the size of the finger.

Technic.—The stump is painted with tincture of iodin. The shaped piece of celluloid, after being soaked in bichloride of mercury (1-1000) for a sufficient time, is sponged off with ether or alcohol. It is then wrapped around the finger and secured with narrow adhesive strips, thus making a tube which is slightly smaller at its free end than at its base. When the tube is properly adjusted it will hug closely the edge of the wound, and will gradually become larger until it impinges on the first interphalangeal joint. The celluloid may extend as far beyond the finger tip as is needful, and in addition to its primary function it also serves as a splint for the finger and as a protection to the wound.

In cases seen early a blood clot is allowed to form in the tube. This clot serves as a scaffold for granulations. If the soft parts are lacerated and spread apart, they are gathered together and held in place by the tube.

In cases seen after the granulations have started, every effort is made to stimulate their growth, and to train this growth along the tube.

Any desired medication may be applied to the wound after the celluloid is in place, either by pouring it into the tube, or by packing the tube with gauze. The dressing in this way comes in contact with the wound, and is confined by the tube. A loose gauze plug is then placed in the mouth of the tube, and over all a small dressing, secured by a bandage.

Summary of Cases.—Fifteen cases. Males, 13; *females*, 2. *Ages*, 16 to 50 years. *White*, 13; *Colored*, 2. *Occupation.*—Operators on machines, 15. *Etiology.*—All were injured by machines. *Situation.*—Right forefinger, 5; left forefinger, 4; right middle finger, 2; left middle finger, 3; right thumb, 1. *Duration of Lesion before coming under my care.*—One hour to 26 days. *Amount Lost.*—From .75 cm. of the tip to the entire terminal phalanx. *Amount Gained.*—From .5 to 1.25 cm. *Type of Lesion.*—The nail was involved in all. In 2 there was some loss of tissue, the remaining soft parts of the terminal phalanx being mush-roomed out and badly crushed, although still attached to the finger by pedicles. In neither of these was the bone involved. In 13 the amputations were more or less clean cut, with little crushing of surrounding tissues, and in all of these the bone was involved. In 10 of these the lesion involved more of the dorsal than of the palmar surface. In 1 the skin was involved equally on both aspects of the finger, and in 2 the lesion involved slightly more of the palmar surface. *Treatment.*—The celluloid tube was used in all, in addition to stimulation. In 1, in addition to the above, small deep grafts were used to hasten healing. *Duration of treatment.*—Entirely healed after 10, 21, 24, 26, 28, 29, 30, 33, 34, 35, 36, 39, 45, and 66 days, with an average of 33 days. The cases taking the greater number of days before healing were those in which the wounds were seen late, and which were prevented from prompt healing in order to give more length to the stump. *Results.*—There is increase in length of the soft parts in all, and in four instances the X-ray showed slight increase in the length of the bone.

There is not a single painful stump in the series. The pad of tissue over the bone is quite movable, and soft in all. Voluntary flexion of the terminal phalanx is excellent in all, even when only a small amount of the phalangeal bone remained. The celluloid tube has also been used with success as a protective dressing for other lesions of the terminal phalanx, such as compound fractures, lacerations, etc.

Remarks.—The accident may be caused in many ways. In this series they were all caused by presses of one sort or another.

The tissue loss of the terminal phalanx varied from that of the soft parts only to that of the entire phalanx.

The lines of section were in varying directions, but the involvement was usually more on the dorsal than on the palmar surface.

There was no retraction of the edges, the sections being as though cut through a banana or a sausage.

The comparative value of the different fingers varies with the occupation, but it may be safely stated that the thumb, the index and the middle fingers are the most generally useful.

The method is simple, and the patient can return to his home at once, and do light work after a short time.

A very small gauze dressing around the celluloid suffices. Any jar on the end of the tube is transmitted to the finger behind the wound, much as is the case in an artificial limb, where the weight-bearing portion is not on the end of the stump, but on the normal tissue above it.

The granulations may be observed through the transparent celluloid without having to remove the tube.

There is sometimes sweating of the skin of the finger, if the tube is allowed to remain in place for longer than two or three days. The tube may be easily removed as it does not stick, and after cleansing, it may be replaced, or a fresh tube adjusted.

The thickness of the granulating area can be stimulated by various means. As the granulations grow, the epithelium from the skin edge also grows, and often it is difficult to prevent it closing over the stump before the desired length is obtained. In these instances the epithelial edges should be retarded with silver nitrate.

In some cases when the granulations are sufficiently advanced, it is advisable to cover them with small deep grafts, in order to give a more stable and quicker healing. It might have been better to have grafted more of this series.

The cases seen soon after the accident give the best results, as far as increased length is concerned.

Building new tissue on the end of the stump is slow, but in the end it will preserve the bone which remains, and cover it; and will also often add materially to the length of the stump. If the joint is uninvolved, even a short bit of terminal phalangeal bone will form the basis for a shortened terminal phalanx, which may be voluntarily extended and flexed, and can be used nearly as well as an intact terminal phalanx.

From the standpoint of function, increased length, and improved appearance, the results have been better than with any other method with which I am familiar.

DISCUSSION.

DR. SMITH: I have been very much interested in this work of Dr. Davis. These cases he has presented this evening would under ordinary circumstances have been treated in the dispensary with good results, but with a shortened finger. By this treatment, a finger practically normal in length has been obtained, which in some cases would undoubtedly mean the difference between efficiency and inefficiency at the patient's trade or employment.

Dr. Davis and his associates have been giving special attention to another class of cases with equally beneficial results. For example, those patients who have slow healing wounds and chronic leg ulcers, many of whom have been returning to the dispensary more or less regularly for months, and in some instances years. They form the uninteresting cases in whom no one has had any particular interest, with the result that they received more or less superficial attention. As soon as Dr. Davis began to study wound healing and took over this work, the results were most gratifying. Many of those old cases were completely healed, and the length of time required for the process in practically any case has been reduced to a minimum. That is efficiency, because it saves the time and the feelings of the patient, besides saving the time of the surgeons and also materials. To members of the working class, the saving of time alone is of great importance. I wish we could have the same efficient methods throughout our dispensary, for there is need of it. The superficial examination and routine treatment characterizing most dispensary work is altogether wrong.

2. * Lesions Produced by Arsenicals and Their Bearing on the Problem of a Specific Arsenic Therapy. DR. WADE H. BROWN.

* To appear later in the BULLETIN.

MAY 17, 1915.

1. Case of Interstitial Omental Hernia and Sarcoma of the Body of the Uterus in the Same Individual. MR. BENJAMIN TAPPAN.

The patient, a white woman, aged 53, married, was admitted to the gynecological service of The Johns Hopkins Hospital on December 2, 1914, complaining of bleeding from the vagina. There was no history of cancer or tuberculosis in her family, and in other respects also her family history was negative. In her personal history her general health was excellent. She suffered from frequent frontal headaches, had occasional attacks of indigestion and sometimes had palpitations of the heart. She had been married twice, but had had no children and no miscarriages. Twenty-five years ago she underwent an abdominal operation, in which she thinks her left ovary was removed. She had no trouble following the operation, except that after several years a small hernia appeared at the lower angle of the scar. This became about as large as a hen's egg and remained stationary in size ever since. It had never at any time given her any trouble and had never been tender or painful. Twelve years before admission the patient was operated upon for hemorrhoids, with relief of the condition. The patient's menses appeared at the age of 12 and continued regularly and with no pain until her menopause, which occurred ten years before her admission to the hospital, at the age of 43. Since then she had had no bleeding at all until her present illness.

Her present illness began a little over a month before her admission to the hospital. She had had for some weeks a leucorrhœa, which was becoming gradually more profuse. One month before her admission she noticed bleeding from the vagina. This bleeding, the first since her menopause ten years before, was never severe. There was only a little bleeding from day to day, just enough to soil her linen. At this time her leucorrhœa became more profuse. She had no other symptoms; her appetite remained good, she felt well and had lost no weight. Her physical examination on admission showed her to be a well-nourished, healthy looking woman. Her lungs were negative. Her heart was slightly enlarged to the left, but there were no murmurs. On the abdomen there was a mid-line scar below the umbilicus, which was well healed, except at its lower portion, where there was a small protrusion, the size of a hen's egg. This protrusion was soft and fluctuant and increased slightly in size when she stood up. It was not tender and never gave her any pain. In other respects her abdominal and general physical examination was negative. The clinical examinations were negative. Vaginal examination, done under anesthesia, just before operation, showed normal external genitalia and vagina. The cervix was high in the vault, small and slightly lacerated. The uterus was normal in size, anteflexed and freely movable. There was no point of induration and no masses were felt. The adnexa seemed free.

She was operated upon on December 5 by Dr. Thomas S. Cullen at The Johns Hopkins Hospital. A curettage was done and the tissue fragments examined under the microscope. The diagnosis of carcinoma was made. The old abdominal scar was first resected. The small hernial sac was opened and proved to be a tri-locular affair, lined with peritoneum and completely filled with omentum. The hernia emerged through a small opening in the old mid-line scar, half way between the umbilicus and the symphysis pubis. It bulged out in a spherical pouch beneath the subcutaneous fat, forming the small tumor which could be felt before opening the abdomen. From this pouch, three long, finger-like processes extended, which lay anterior to the anterior sheath of the rectus muscle and the aponeurosis of the external oblique muscle, and underneath the subcutaneous fat. The upper one burrowed to the right in a horizontal direction almost to the anterior superior spine of the ileum. The middle one extended obliquely to the right to Poupart's ligament, and the lower one reached down vertically in the mid-line almost to the symphysis pubis. None of

these finger-like processes could be felt from the outside, as they were flattened anteroposteriorly. They widened out considerably, however, in the other diameter and measured at the widest points from about 3 to 6 cm. The peritoneum covering the hernia was very adherent to the omentum which filled the sac and to the subcutaneous fat above it.

The pelvic viscera as seen through the wound showed that both tubes had been amputated previously. The uterus was of normal size and appearance. A double oophorectomy and a panhysterectomy were done. The hernial sac was then resected. The operation took two hours. The patient made an uneventful recovery and was discharged in good condition on January 1, 1915.

The uterus after removal appeared perfectly normal. Upon section, however, there was seen in the fundus a grayish, cauliflower mass, the size of a marble, which on examination was seen to have grown from the posterior wall of the uterus near the fundus. This growth resembled very closely a carcinoma and was thought to be a carcinoma, although the processes of the tumor were a little blunter and larger than in a typical carcinoma. There was no evidence in the gross of extension of the mass or of a metastases. There was no area of necrosis in the growth. There was in the anterior wall of the uterus a small subserous myoma about 4 cm. in diameter. Microscopical section of the tumor mass in the fundus showed it to be made up of large, spindle-shaped cells, running irregularly in parts, and in parallel strands in other parts. The cells were very uniform in size, had oval vesicular nuclei and were separated by a small amount of stroma. There were small capillaries between the cells. The pathological diagnosis was spindle-celled sarcoma of the body of the uterus. The endometrium showed a chronic endometritis and there was hypertrophy of the glands. There was considerable round-celled infiltration of the tumor mass. The mass did not appear to be invasive and there were no metastases seen.

2. A Case of Myoma of the Appendix. Dr. G. L. Stickney.

Mrs. S., age 39, who had for a year previous to operation complained of symptoms of chronic appendicitis, was operated upon on January 25, 1915. At operation a small clubbed appendix was found adherent to the right tube. Both structures were removed.

The appendix measured 5 cm. in length. Its diameter for a distance of 3.5 cm. from its base was uniform, measuring 7 mm., from this point it terminated in a clubbed extremity 1.5 cm. in length and 11 mm. in diameter. On section it was found to be a circumscribed solid tumor, in which a lumen could not be demonstrated.

Histologically the clubbed extremity was composed of five small circumscribed myomata, the largest measuring 3.5 mm. in diameter one situated on either side of the lumen, and three placed about the periphery.

The tumors were composed of nonstriated muscle fibers. Surrounding them generally was a loose connective tissue capsule, which in places was absent. Here the interlacing between the muscle fibers of the appendix wall and those of the tumor was so indeterminate that it was difficult to differentiate the two.

The lumen was represented by a cresent-shaped figure compressed between two myomata, which had become obliterated except at one extremity, where it was of microscopic size, and its lining epithelium intact. The mucosa was densely infiltrated with inflammatory exudate.

The subserosa was thickened, showing fibrous-tissue proliferation and many new-formed blood vessels. This connective-tissue proliferation had extended in between the muscle fibers of the external coat and the myomata. A review of the literature revealed a total of 647 cases of tumor of the appendix, of which only three were found to be myomata.

3. A Case of Diffuse Adenomyoma of the Uterus, with Discrete Adenomyoma over the Left Ureter. Dr. G. L. Stickney.

Adenomyoma of the female pelvic organs, other than that of the uterus, forms a small proportion of the total number of cases. From the specimens examined in the gynecological laboratory of this clinic, one finds a proportion of 1 to 13 in a total of 183 cases.

The following case presents a diffuse adenomyoma of the uterus with a discrete circumscribed adenomyoma over the left ureter. The patient, an unmarried woman aged 36 years, for a year previous to entrance into the hospital, had complained of a dull pain over the lower abdomen, which later was referred to the rectum, and which was accompanied with a profuse leucorrhœa.

At operation a small myomatus uterus was found. A nodule was also found in the base of the left broad ligament, simulating a ureteral calculus. After a supra-vaginal hysterectomy, the left ureter was dissected free for a distance of 2 cm., and at a point about 1 cm. from the crossing of the uterine artery there was found on its anterior surface a small tumor 1 cm. in diameter which was dissected free and removed.

The uterus, besides containing many circumscribed myomata, showed a diffuse adenomyoma.

The tumor removed from the region of the left ureter is composed of nonstriated muscle fibers, surrounding two small islands of gland structure, the glands being lined with a single layer of cylindrical epithelium, and surrounded by a cellular connective tissue, presenting a picture similar to that of the uterine mucosa.

4. Small Bony Mass Lying on the Posterior Surface of the Right Broad Ligament. Dr. Wm. Neill, Jr.

Mrs. B., age 35 years. Occupation, hairdresser. Nationality, American. Admitted into C. H. I., March 4, 1915.

Complaint.—Pain in lower abdomen.

Family History.—Negative.

Past History.—General health good. No serious illnesses.

Present Illness.—Patient dates her trouble from a miscarriage in 1905.

Duration of this pregnancy, five months. A curettage was done about a week later. Following this, from three to four years, she had considerable pain in the lower left side of her abdomen. Her menstrual periods during this time were also irregular.

Two years ago, in the fall of 1913, while driving an automobile, she was taken suddenly with a sharp cutting pain in the lower right side of her abdomen. This was so severe as to demand morphia. This lasted three days, and for several weeks afterwards she had the sensation as of a mass pushing itself through on this side. Was well after this until October, 1914. From then on she felt badly all over. Could only work three or four days a week. Suffered with headache and pains across the lower abdomen and down the thighs. General lassitude. These symptoms gradually became more marked. At her menstrual period in both January and February, 1915, she had severe cramps over the abdomen, which were accompanied by a profuse yellowish leucorrhœa. This latter complaint continued up to the time of admission.

Examination on Admission.—The patient is a healthy looking woman, complaining of pain in lower abdomen. Heart and lungs negative. The abdomen is full and soft. Moderate tympany all over. Quite tender on pressure in lower left quadrant. No masses or muscle rigidity made out. Further examination negative.

Vaginal Examination.—The outlet is firm, cervix normal. A mass about 12 cm. in diameter is felt on left side of uterus. Fundus normal size, moderately backward, and only slightly movable. On the right side a small hard mass is felt, about two inches above the cervix. This is movable.

Rectal Examination.—Vaginal examination was confirmed. The same hard nodule is felt on the right side and behind, near the

cervix. It is so movable that it can be delivered outside the anal orifice with two fingers in the vagina and one in rectum.

Temperature and pulse normal. Urine negative. No leucocytosis.

Operation.—March 6, 1915. On the left side of the uterus, a tubo-ovarian cyst about 10 cm. in diameter was encountered. This was removed with great difficulty, owing to the density of adhesions. On the right side, all that remained of the tube was a stump about 2 cm. long. This was completely imbedded in the broad ligament. There was no trace of any ovary. It looked just as if both tube and ovary had been removed at a previous operation. There were no adhesions. There had evidently been a spontaneous amputation of both the ovary and tube.

Slightly below the point where the ovary should have been was a flat triangular plaque about 2.5 cm. on each side and about 1 cm. thick. This was very hard and proved to be the mass that could be pushed out through the rectum when the patient was examined under ether. It was covered by adhesions, but it was possible to shell it out without producing hemorrhage. In fact, it was shelled out without a suture or ligature being applied.

Sections from this tissue were found to consist entirely of new-formed bone. No trace of ovarian tissue was demonstrable.

Origin.—Of course the most natural conclusion would be that the bone originated from the ovary, which had been spontaneously amputated with its corresponding tube. This explanation is the most plausible one. On the other hand we have no evidence of any ovarian tissue from this side and it is difficult to explain the presence of such normal looking bone when all vestige of ovarian tissue has disappeared. As a matter of fact, we cannot explain, satisfactorily, the presence of this bone, which was so firmly attached to the posterior surface of the broad ligament just 2 to 3 cm. below the site of the normal right ovary.

5. An Interesting Case of Tuberculosis of the Ileum from a Diagnostic Standpoint. DR. WM. NEILL, JR.

Miss H., age 17 years. Nationality, American. Admitted September 25, 1914, into the C. H. I. Surgical No. 11731. Discharged December 3, 1914.

Complaint.—Pain in right side of abdomen.

Family History.—Negative.

Past History.—General health good, prior to present illness.

Present Illness.—Beginning in the spring of 1912, patient has had a constant diarrhœa. From three to four liquid stools a day. No nausea or vomiting or abdominal pain. Never noticed any blood or mucus in stools. In February, 1914, she had an attack of abdominal colic, with nausea and vomiting. Had similar attacks during the following March and May. In August, 1914, she began having indefinite pain in the epigastrium. This lasted a week or ten days, then gradually extended downwards and localized itself in the lower right quadrant of the abdomen. This pain was a constant, dull ache, which at times became severe and caused nausea and vomiting, which seemed to relieve it. Has gotten weaker and lost all appetite. Has seen several physicians and at no time has a definite diagnosis been made.

The diarrhœa has continued. Has been running a slight elevation of temperature for the past two months. Has lost about 16 pounds in weight.

Present Examination.—Fairly well nourished girl slightly anæmic. Chest negative. There is a slight abdominal fullness in the lower right quadrant. A definite mass can be felt here, measuring 5 x 10 cm., indefinite in outline and lying close to pelvis. Quite painful. Rt. rectus muscle held rigid. The mass is firm and percussion note over it is dull. Not movable. Not adherent to the skin. On rectal examination, there is thickening on right side. Pelvic organs negative

Urine negative. W. b. c. 19150. Hb. 55 per cent. Stools contain trace of blood. No mucus, parasites, or ova. Wassermann negative. Temperature 101°.

Operation.—September 26, 1914. A McBurney incision was made over the mass. As soon as the skin was incised, the tissues were found indurated, and this became more marked as the layers were divided. On reaching the peritoneum, it was found to be adherent to a large mass about 12 cm. in diameter. Dissection was carried on extra-peritoneally and a pocket of thick, yellowish pus evacuated, about 30 cc. The operation ceased here, as the tissues were so indurated it was not possible to separate them. A small piece of tissue was removed, which on section, proved to be only chronic inflammatory tissue. Drains were placed down to the abscess and a diagnosis of appendiceal abscess made.

The patient drained profusely and a fecal fistula developed several days later. Bismuth paste was tried without success. On leaving the hospital December 3, 1915, she had improved in health and strength. Appetite had returned, and her bowels were now regular. The mass had disappeared. She returned to the hospital regularly for dressings and all this time continued to have a fecal discharge from the fistula. It was hoped that the fistula would close itself, for it was realized that a second operation to close it would mean an extensive and dangerous undertaking.

Patient was readmitted into the hospital January 24, 1914, for the purpose of closing the fistula, as it gave no signs of closing spontaneously.

On examination, patient was much improved in health. The fistula remains open and drains freely. Bowels are regular and contain no blood or mucus.

The second operation was performed by Dr. Cullen, January 25, 1915. The fistula was closed and placed outside of the operative field. A rt. rectus incision was made. Dense adhesions had to be freed everywhere before the cæcum and ileum could be loosened. Much to the surprise of everyone, the appendix was found intact. It was thickened throughout its length but at no point did it show any evidence of ulceration. It was removed.

A hole, about 1 cm. in diameter, was found in the small bowel about 2 inches from its junction to the cæcum. This connected with the fistulous tract. On attempting to close this perforation, the tissue was found to be so thickened, that had it been possible to close it, in all probability intestinal obstruction would have resulted. The bowel was markedly thickened for a distance of about 8 inches upwards. A resection of this portion was thought advisable, as it was so badly diseased and also in view of the fact that the perforation could not be closed with any degree of safety. This was done. The two ends of the remaining bowel turned in and a lateral anastomosis performed between the last portion of the ileum and cæcum. The fistulous tract excised and a drain placed down through this opening to the cæcum. The rt. rectus incision closed without draining.

The excised portion of gut was markedly thickened, but nothing else noteworthy could be determined. A diagnosis of perforated typhoid ulcer was made, with a question mark. Sections of this tissue showed tuberculosis.

The patient has made an uneventful recovery, with the exception of small superficial abcesses forming in the old McBurney incision at various intervals. Both incisions to date are healed firmly and the patient is in excellent health.

6. An Interesting Case of Appendicitis. DR. T. STARR.

Surgical No. 12820. Mrs. K. H., age 45 years. Admitted to the Church Home and Infirmary, April 30, 1915, complaining of a mass in the right groin.

Past History.—Negative, except for the following facts:

Patient has had a hernia since girlhood. At first, it was very soft, and easily reducible. She suffered from a constant, dull

sensation in right groin when standing, some pain when walking, but this discomfort was relieved by wearing a support.

About 14 years ago, she was taken with most intense pain across the lower abdomen. Pains were cramplike in character and gradually became localized over lower right abdominal quadrant. She was nauseated and vomited frequently.

The hernia, and the area surrounding it over a surface about the size of palm of hand, became very sensitive to touch. She had several distinct chills and probably had fever. Bowels were constipated. After a few days, the pains subsided but the hernial area remained very sensitive for about three weeks.

After recovery, patient noticed that she had more difficulty in reducing hernia than formerly and was unable to reduce the entire swelling. For the past nine years, it has been irreducible.

Since this attack, she has been able to do her usual work, but has not felt well. Appetite has been poor and she has suffered much with indigestion and constipation. For a year she suffered every evening with nausea and vomiting, but has had no such symptoms during past two years. Five weeks before admission, following considerable exercise, patient noticed that the hernia was more sensitive to pressure than usual and that stooping forward caused much pain in this region.

The next day, she had an attack similar to illness 14 years before. She suffered first with very severe abdominal cramps, general in distribution. These gradually became localized over the hernia and the immediately adjacent areas. Pain was so severe that numerous injections of morphia were required. Pressure over lower right abdominal quadrant was accompanied by much discomfort. She suffered from persistent diarrhœa for two weeks, but no vomiting.

After about two weeks, the pain began to subside, and on admission to the hospital she suffered only when considerable pressure was applied over hernia.

On examination, a woman past middle age, who appeared rather ill, was found. Examination of heart and lungs was negative. In the right groin, just beneath Poupart's ligament, there was a very firm tumor about the size of a hen's egg. Tumor was round or oval in shape and was movable to a limited extent in all directions. It was very superficial and appeared to be attached to the overlying skin. Tracing it upward, its size became reduced to a smaller neck and this apparently passed through femoral ring into abdominal cavity. There was no impulse on coughing nor could the size of the mass be reduced by pressure. There was no evidence of inflammatory reaction except some tenderness on pressure and this extended as far upward as the level of the umbilicus. There was no elevation of temperature.

Urinary examination was negative.

Patient was operated upon on May 1, 1915, by Dr. Cullen. A midline incision was made, in order to suspend the uterus. A piece of omentum, the size of a pigeon's egg, was found plugging the left inguinal ring. This was removed and amputated. Ring was closed with catgut.

It was found that the cæcum was drawn down to the right femoral ring and that the appendix passed through the ring and lay extra-abdominally, within the hernial sac. There was also a mass of omentum and fat, the size of a hen's egg, intimately surrounding the appendix. This was so adherent that it was not possible to reduce the appendix into abdomen. An incision was made over the hernia, and the sac was freed from the surrounding tissues. In order to reduce the mass, it was necessary to enlarge the ring by cutting through Poupart's ligament. The peritoneum was then split down to the ring and the hernial mass was drawn into the abdominal cavity. The cæcum was well surrounded with gauze and appendectomy was done with cautery. Poupart's ligament was repaired with kangaroo tendon. Hernial opening was closed with mattress sutures of kangaroo on liver needles. Closure without drainage.

Patient has made an uneventful recovery.

Pathological specimen is a firm, kidney-shaped mass, 6 cm. x 3 cm. x 3 cm. Its surface is somewhat nodular and is covered with peritoneum. Corresponding to the hilum of a kidney, a considerably thickened appendix with its mesentery is seen entering the mass. On section, a very much thickened and indurated hernial sac, surrounded by preperitoneal fat, is seen. The appendix is buried in the fatty tissue near the periphery.

7. A Study of the Relation Between the Degree of Menstrual Reaction in the Endometrium and the Clinical Character of Menstruation. (Abstract.) Dr. Emil Novak.

This study is based upon a review of some 2000 clinical cases in the gynecological department of The Johns Hopkins Hospital. From these were selected all those in which the endometrium had been removed, either by curettage or by hysterectomy. The number of these was 339. By eliminating a number which for one reason or another were not suited for the purpose of this study, the number was reduced to 268. The entire number of cases was now easily divisible into two main groups, viz. (1) those in which menstruation, whatever its other clinical variations may have been, still retained its regular periodicity; (2) those in which the menstrual rhythm had been broken, the periods recurring at irregular intervals. This study is based upon the 159 cases of the first group, the remainder being obviously unsuitable for an investigation in which the chronology of the menstrual cycle plays such an important part.

The point of departure in any modern study of the menstrual histology of the endometrium must be the epoch-making contribution of Hitschmann and Adler, published in 1908. These investigators showed clearly that the endometrium undergoes a gradual and progressive development from the end of one menstrual period to the beginning of the next, so that its appearance varies from day to day. These developmental changes are especially characterized by a progressive hypertrophy of the glands, reaching its high point just before the onset of menstruation, in the so-called premenstrual period. Less constant and less conspicuous hypertrophic changes are noted in the stroma. The study of a large number of endometriums impresses one with the marked individual differences in the degree of these hypertrophic changes, especially in the glands. Do these differences correspond to the well-known individual differences in the clinical intensity of the menstrual flow?

The study suggested by this query must be one of comparison, and the first essential is that only those endometriums may be compared which have been removed on corresponding days of the menstrual cycle. This was accomplished by dividing the entire number of cases into groups, according to the day of the menstrual cycle on which the endometrium was removed. The first day of menstruation, being the only fixed date, was designated as the first day of the cycle. Precautions were taken to obviate or at least minimize the personal factor in the investigation.

The study of this rather large series of cases indicates, first of all, the general correctness of the teaching of Hitschmann and Adler as to the cyclical histological variations in the endometrium at different periods of the menstrual cycle. An interesting relation is shown to exist between the clinical character of the menstrual flow and the degree of endometrial hypertrophy called forth by the menstrual stimulus. Speaking generally, the more profuse the menstrual flow, the more marked the local hypertrophic changes in the endometrium. The less abundant the flow, the less striking the local reaction in the endometrium. The latter must therefore be looked upon as playing an essentially passive rôle in menstruation.

An important exception to the above generalization is en-

countered in cases of anteflexion of what is commonly spoken of as the congenital type. In the 33 cases of this group, hypertrophic changes are, if anything, more marked than those noted in association with other pelvic conditions, even though menstruation is frequently scanty. This would indicate that the ovary, whose activity appears to govern the degree of menstrual hyperemia and the associated endometrial hypertrophy, is not functionally deficient in such cases, as has so frequently been stated. The scanty menstruation so commonly observed in cases of this type is perhaps due to a deficiency in a local factor whose activity permits of the passage of blood elements from the vessels toward and into the uterine cavity. Such a theory would seem to explain the spasmodic dysmenorrhea so characteristic of congenital anteflexion, for the engorged mucosa, acting as an irritant to the uterine musculature, gives rise to painful spasmodic contractions of the latter, until relieved by the onset of the menstrual flow. A physiological, rather than an anatomical, deficiency in the endometrium may also in some as yet unknown way be responsible for the sterility which is frequently seen in association with congenital anteflexion.

NOTES ON NEW BOOKS.

A Manual of Obstetrics. By EDWARD P. DAVIS, A. M., M. D. Cloth, $2.25. (*Philadelphia: W. B. Saunders Company, 1914.*)

With the large number of excellent text-books on obstetrics already available, it does not seem that this volume supplies any particular need in this branch of medicine.

It is to be regarded merely as a handbook, the various subjects taken up being considered in the briefest manner. The author almost entirely neglects the scientific aspect, and tends to assume rather too didactic an attitude when considering the various unsolved problems met with in obstetrics.

In view of the brief and perfunctory manner in which the author treats of the various abnormalities encountered in obstetrical practice, it is difficult to see that the book will prove of very great value either to the student or practitioner.

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This volume contains 29 articles of greater or less length on medicine, surgery, diagnosis and treatment, and medico-legal and miscellaneous topics. Three of them relate to radium, one to painless childbirth, another to the routine administration of ether in measured dosage, all of which just now are of vital interest to the profession.

"A Visit to the Mayo Clinic at Rochester, Minnesota" fills up 25 pages and is attractively illustrated. It gives the special methods and treatment employed in Rochester.

An article of the same general character on the "London Clinical Congress of Surgeons," recently held in London, describes some of the methods of operating in London.

Another article by Max Broedel on "Medical Illustration" gives desirable and valuable information as to the preparation of illustrations for medical and surgical papers and the instruction of the student in drawing.

I. K. Therapy, with Special Reference to Tuberculosis. By W. E. M. ARMSTRONG, M. D. Cloth, $1.50 net. (*New York: Paul E. Hoeber, 1914.*)

This book contains a brief account of the theoretical speculations on which Spengler bases his *Immun-körper* (serum) treatment of tuberculosis, and a general outline of the methods laid down by him for controlling the treatment of patients. The experimental and clinical data supporting his theories are given in such a superficial sketchy way, that the reader is quite unable to draw any conclusions for himself as to their reliability. The book has been written evidently by an enthusiast with very little critical insight into the immunological problems involved. In view of the fact that Spengler's fantastic theories have found no corroboration on the part of other investigators of recognized ability, and since the scanty clinical observations adduced in support of the treatment are far from convincing, it would seem that there is as yet no justification whatever for attempting to bring this method of treatment into general use.

A Course in Normal Histology. Vols. I and II. By RUDOLF KRAUSE. Translated from the German by PHILIP J. R. SCHMAHL, M. D. (*New York: Rebman Company, 1913.*)

This may certainly be regarded as among the noteworthy text-books lately published.

The first volume is devoted to the technique of microscopy. It includes an explanation of the microscope, a presentation of the methods for the preparation of microscopic specimens, including injection, impregnation, staining and mounting, together with the principles of mensuration and drawing. The use of the camera lucida is described under the last sub-heading.

The text is clear and concise. Its value is augmented by admirable diagrams and illustrations which facilitate the understanding of the microscope as well as supplying the essentials of microscopic examination.

The second volume is an atlas of normal histology and may be very highly recommended as a supplement to a good text-book.

The text is divided into three general parts devoted, respectively, to the cell, the different types of animal tissues and the structure of organs. The text is illustrated with 208 colored plates which are reproductions of the original drawings in Krause's book and are, for the most part, very good.

Krause's original work is too well known to require any comment. The translation is excellent. Each volume is in itself complete and may be used to advantage independently of the other.

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